SEARCH NOTES 10/603,369 3/2/05

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	8	("6284763" "6458797" "6787553" "6326379" "6576644").pn.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 14:04
L2	2	"6087368".pn.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 13:38
L3	49	"PDE5" near5 "IC50"	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 14:20
L4	30	"PDE5" near5 "IC50" near5 ("100" or "50")	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 14:19
L5	0	l4 not l3	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 14:19
L6	0	l2 and "IC50"	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 14:22
L7	2	"6048864".pn.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 14:22
L8	0	l7 and "IC50"	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 14:22
L9	5	("6103738" "6169093" "6365599").pn.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 14:23
L10	0	l9 and "IC50"	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 14:23

L11	0	l9 and "IC"	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 14:27
L12	0	ep-0463756-$.did.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 15:28
L13	2	wo-9519978-$.did.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 14:31
L14	14844	"IC50"	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 14:32
L15	162	phosphodiesterase same l14	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 14:32
L16	159	l15 not l3	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 14:37
L17	44	l15 and hypertension	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 15:02
L18	2	wo-9808848-$.did.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 15:03
L19	2	wo-9703675-$.did.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 15:05
L20	2	wo-9703985-$.did.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 15:07

L21	2	wo-9719947-$.did.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 15:14
L22	2	wo-9724334-$.did.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 15:12
L23	2	"5488055".pn.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 15:12
L24	2	wo-9518097-$.did.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 15:14
L25	2	wo-9807430-$.did.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 15:14
L26	54474	(hypertension or (high adj blood adj pressure))	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 15:15
L27	0	ep-A0463756-$.did.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 15:28
L28	0	ep-0463756A-$.did.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 15:28
L29	0	ep-A463756-$.did.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 15:29
L30	2	ep-463756-$.did.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 15:57

L31	355	saralasin	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 15:57
L32	319	l31 and angiotensin$	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 15:58
L33	278	l32 and hypertension	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 17:44
L34	15	(sildenafil adj citrate) same hypertension	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 17:48
L35	54	candesartan and eprosartan and irbesartan and losartan and olmesartan$ and telmisartan and valsartan	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 17:51
L36	4	("4355040" "4880804").pn.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 17:51
S1	3	("cGMP" or (cyclic adj guanosine adj monophosphate)) near5 (phosphodiesterase$ or "PDE5") same (angiotensin near3 (receptor adj antagonist))	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/01 16:46
S2	14	("cGMP" or (cyclic adj guanosine adj monophosphate)) near5 (phosphodiesterase$ or "PDE5") and (angiotensin near3 (receptor adj antagonist))	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 09:58
S3	3	("6458797" "6284763").pn.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/01 17:07

S4	19727	sildenafil or viagra or tadalafil or "IC-351" or "IC 351" or cialis or vardenafil or levitra or candesartan or "CV-11974" or "CV 11974" or eprosartan or teveten or "SKF-108566" or "SKF 108566" or irbesartan or "BMS-186295" or "BMS 186295" or "SR-47436" or "SR 47436" or avapro or aprovel or karvea or losartan or cozaar or "dup-753" or "dup 753" or "MK-954" or "MK 954" or (olmesartan adj medoxomil) or "CS-866" or "CS 866" or benicar or olmetec or votum or saralasin or "P-113" or "P 113" or telmisartan or "BIBR 277" or "BIBR277" or "BIBR-277" or pritor or micardis or valsartan or diovan or "CGP-48933" or "CGP 48933" or "CGP48933" or tareg or kalpress or miten or nisis or provas or vals	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/01 17:20
S5	1458	sildenafil or viagra or tadalafil or "IC-351" or "IC 351" or cialis or vardenafil or levitra	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/01 17:19
S6	18588	candesartan or "CV-11974" or "CV 11974" or eprosartan or teveten or "SKF-108566" or "SKF 108566" or irbesartan or "BMS-186295" or "BMS 186295" or "SR-47436" or "SR 47436" or avapro or aprovel or karvea or losartan or cozaar or "dup-753" or "dup 753" or "MK-954" or "MK 954" or (olmesartan adj medoxomil) or "CS-866" or "CS 866" or benicar or olmetec or votum or saralasin or "P-113" or "P 113" or telmisartan or "BIBR 277" or "BIBR277" or "BIBR-277" or pritor or micardis or valsartan or diovan or "CGP-48933" or "CGP 48933" or "CGP48933" or tareg or kalpress or miten or nisis or provas or vals	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/01 17:20
S7	42	(S5 and S6).ti,ab,clm.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/01 17:21

S8	319	S5 and S6	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/01 17:21
S9	128	S8 and (hypertension or (high adj blood adj pressure))	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/01 17:41
S10	2	"6576644".pn.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/01 17:41
S11	1458	sildenafil or viagra or tadalafil or "IC-351" or "IC 351" or cialis or vardenafil or levitra	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 09:58
S12	18588	candesartan or "CV-11974" or "CV 11974" or eprosartan or teveten or "SKF-108566" or "SKF 108566" or irbesartan or "BMS-186295" or "BMS 186295" or "SR-47436" or "SR 47436" or avapro or aprovel or karvea or losartan or cozaar or "dup-753" or "dup 753" or "MK-954" or "MK 954" or (olmesartan adj medoxomil) or "CS-866" or "CS 866" or benicar or olmetec or votum or saralasin or "P-113" or "P 113" or telmisartan or "BIBR 277" or "BIBR277" or "BIBR-277" or pritor or micardis or valsartan or diovan or "CGP-48933" or "CGP 48933" or "CGP48933" or tareg or kalpress or miten or nisis or provas or vals	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 09:58
S13	319	S11 and S12	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 09:58
S14	128	S13 and (hypertension or (high adj blood adj pressure))	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 09:58

S15	128	S14	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 09:59
S16	115	S15 and ((congestive adj heart adj failure) or angina or stroke or diabet$)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 10:00
S17	0	S16 not S15	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 10:01
S18	1451	sildenafil or viagra or tadalafil or cialis or vardenafil or levitra	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 10:02
S19	1767	candesartan or eprosartan or irbesarta or losartan or olmesartan or (olmesartan adj medoxomil) or saralasin or telmisartan or valsartan	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 10:04
S20	42	(S18 and S19).ti,ab,clm.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 10:03
S21	42	(S11 and S12).ti,ab,clm.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 10:04
S22	0	S20 not S21	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 10:04
S23	1821	candesartan or eprosartan or irbesartan or losartan or olmesartan or (olmesartan adj medoxomil) or saralasin or telmisartan or valsartan	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 10:04
S24	42	(S18 and S23).ti,ab,clm.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 10:05

S25	0	S24 not S20	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 10:05
S26	310	S18 and S23	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 10:05
S27	187	S26 and (hypertension or hypertensive or (high adj blood adj pressure))	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 10:05
S28	164	S27 not S24	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 10:06
S29	53	S28 not S15	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 10:45
S30	210	S26 and ((congestive adj heart adj failure) or angina or stroke or diabet$)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 10:45
S31	192	S30 not S24	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 10:46
S32	86	S31 not S15	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 10:46
S33	139	S31 not S29	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 10:46
S34	33	S32 not S29	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 13:27

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SEARCH NOTES

10/603,369

3/2/05

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NEWS	4	OCT 28	KOREAPAT now available on STN
NEWS	5	NOV 30	PHAR reloaded with additional data
NEWS	6	DEC 01	LISA now available on STN
NEWS	7	DEC 09	12 databases to be removed from STN on December 31, 2004
NEWS	8	DEC 15	MEDLINE update schedule for December 2004
NEWS	9	DEC 17	ELCOM reloaded; updating to resume; current-awareness alerts (SDIs) affected
NEWS	10	DEC 17	COMPUAB reloaded; updating to resume; current-awareness alerts (SDIs) affected
NEWS	11	DEC 17	SOLIDSTATE reloaded; updating to resume; current-awareness alerts (SDIs) affected
NEWS	12	DEC 17	CERAB reloaded; updating to resume; current-awareness alerts (SDIs) affected
NEWS	13	DEC 17	THREE NEW FIELDS ADDED TO IFIPAT/IFIUDB/IFICDB
NEWS	14	DEC 30	EPFULL: New patent full text database to be available on STN
NEWS	15	DEC 30	CAPLUS - PATENT COVERAGE EXPANDED
NEWS	16	JAN 03	No connect-hour charges in EPFULL during January and February 2005
NEWS	17	FEB 25	CA/CAPLUS - Russian Agency for Patents and Trademarks (ROSPATENT) added to list of core patent offices covered
NEWS	18	FEB 10	STN Patent Forums to be held in March 2005
NEWS	19	FEB 16	STN User Update to be held in conjunction with the 229th ACS National Meeting on March 13, 2005
NEWS	20	FEB 28	PATDPAFULL - New display fields provide for legal status data from INPADOC
NEWS	21	FEB 28	BABS - Current-awareness alerts (SDIs) available
NEWS	22	FEB 28	MEDLINE/LMEDLINE reloaded
NEWS	23	MAR 02	GBFULL: New full-text patent database on STN

NEWS EXPRESS JANUARY 10 CURRENT WINDOWS VERSION IS V7.01a, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 10 JANUARY 2005

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FILE 'HOME' ENTERED AT 11:49:08 ON 02 MAR 2005

=> file caplus
COST IN U.S. DOLLARS

	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

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FILE COVERS 1907 - 2 Mar 2005 VOL 142 ISS 10
FILE LAST UPDATED: 1 Mar 2005 (20050301/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> e fox david/au

E1	3	FOX DARRELL EUGENE/AU
E2	2	FOX DAVE/AU
E3	44 -->	FOX DAVID/AU
E4	49	FOX DAVID A/AU
E5	9	FOX DAVID B/AU
E6	1	FOX DAVID BRIAN/AU
E7	2	FOX DAVID C/AU
E8	1	FOX DAVID CHARLES/AU
E9	1	FOX DAVID D/AU
E10	1	FOX DAVID E/AU
E11	1	FOX DAVID H/AU
E12	1	FOX DAVID III/AU

=> e

E13	39	FOX DAVID J/AU
E14	1	FOX DAVID JONATHAN/AU
E15	1	FOX DAVID K/AU
E16	6	FOX DAVID L/AU
E17	1	FOX DAVID LEE/AU
E18	1	FOX DAVID LEROY/AU
E19	3	FOX DAVID M/AU
E20	1	FOX DAVID N/AU
E21	12	FOX DAVID N A/AU
E22	10	FOX DAVID NATHAN ABRAHAM/AU
E23	1	FOX DAVID R/AU
E24	1	FOX DAVID S/AU

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=> s e2-e3, e20-e22
              2 "FOX DAVE"/AU
             44 "FOX DAVID"/AU
              1 "FOX DAVID N"/AU
             12 "FOX DAVID N A"/AU
             10 "FOX DAVID NATHAN ABRAHAM"/AU
L1           69 ("FOX DAVE"/AU OR "FOX DAVID"/AU OR  "FOX DAVID N"/AU OR "FOX
                DAVID N A"/AU OR "FOX DAVID NATHAN ABRAHAM"/AU)

=> e hughes bernadette/au
E1            1      HUGHES BENZIE RHIANNON/AU
E2            2      HUGHES BENZIE RHIANNON M/AU
E3           19 --> HUGHES BERNADETTE/AU
E4            3      HUGHES BERNADETTE M/AU
E5           32      HUGHES BERNARD P/AU
E6            4      HUGHES BERNIE P/AU
E7            3      HUGHES BETH/AU
E8            3      HUGHES BETSY/AU
E9            2      HUGHES BETSY J/AU
E10           1      HUGHES BETSY JANE/AU
E11           1      HUGHES BETSY R/AU
E12           1      HUGHES BILL/AU

=> s e3-e4
             19 "HUGHES BERNADETTE"/AU
              3 "HUGHES BERNADETTE M"/AU
L2           22 ("HUGHES BERNADETTE"/AU OR "HUGHES BERNADETTE M"/AU)

=> e hughes b/au
E1            6      HUGHES AUSTIN/AU
E2          158      HUGHES AUSTIN L/AU
E3           40 --> HUGHES B/AU
E4            4      HUGHES B A/AU
E5            1      HUGHES B C/AU
E6            5      HUGHES B D/AU
E7            2      HUGHES B F/AU
E8            7      HUGHES B G/AU
E9            2      HUGHES B H/AU
E10          14      HUGHES B J/AU
E11          21      HUGHES B L/AU
E12          13      HUGHES B M/AU

=> s e3
L3           40 "HUGHES B"/AU

=> e fox d/au
E1            2      FOX CYRIL/AU
E2           27      FOX CYRIL S/AU
E3           75 --> FOX D/AU
E4           25      FOX D A/AU
E5            5      FOX D B/AU
E6           10      FOX D C/AU
E7            3      FOX D E/AU
E8           60      FOX D G/AU
E9            1      FOX D H/AU
E10          18      FOX D J/AU
E11           7      FOX D K/AU
E12          41      FOX D L/AU

=> e
E13           3      FOX D M/AU
E14           6      FOX D P/AU
E15           1      FOX D P S/AU
E16           4      FOX D R/AU
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E17          8      FOX D S/AU
E18         20      FOX D W/AU
E19          8      FOX DALE B/AU
E20          1      FOX DALE BENNETT/AU
E21          5      FOX DANIEL/AU
E22          1      FOX DANIEL A/AU
E23          1      FOX DANIEL G/AU
E24         14      FOX DANIEL J/AU

=> e fox d?/au
E1           8      FOX D S/AU
E2          20      FOX D W/AU
E3           0 --> FOX D?/AU
E4           8      FOX DALE B/AU
E5           1      FOX DALE BENNETT/AU
E6           5      FOX DANIEL/AU
E7           1      FOX DANIEL A/AU
E8           1      FOX DANIEL G/AU
E9          14      FOX DANIEL J/AU
E10          7      FOX DANIEL JOSEPH/AU
E11          8      FOX DANIEL L/AU
E12          1      FOX DANIEL RICHARD/AU

=> d his

     (FILE 'HOME' ENTERED AT 11:49:08 ON 02 MAR 2005)

     FILE 'CAPLUS' ENTERED AT 11:49:13 ON 02 MAR 2005
                E FOX DAVID/AU
L1           69 S E2-E3, E20-E22
                E HUGHES BERNADETTE/AU
L2           22 S E3-E4
                E HUGHES B/AU
L3           40 S E3
                E FOX D/AU
                E FOX D?/AU

=> e fox d/au
E1           2      FOX CYRIL/AU
E2          27      FOX CYRIL S/AU
E3          75 --> FOX D/AU
E4          25      FOX D A/AU
E5           5      FOX D B/AU
E6          10      FOX D C/AU
E7           3      FOX D E/AU
E8          60      FOX D G/AU
E9           1      FOX D H/AU
E10         18      FOX D J/AU
E11          7      FOX D K/AU
E12         41      FOX D L/AU

=> s e3
L4          75 "FOX D"/AU

=> d his

     (FILE 'HOME' ENTERED AT 11:49:08 ON 02 MAR 2005)

     FILE 'CAPLUS' ENTERED AT 11:49:13 ON 02 MAR 2005
                E FOX DAVID/AU
L1           69 S E2-E3, E20-E22
                E HUGHES BERNADETTE/AU
L2           22 S E3-E4
                E HUGHES B/AU
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L3            40 S E3
                 E FOX D/AU
                 E FOX D?/AU
                 E FOX D/AU
L4            75 S E3

=> s l1 or l4
L5           144 L1 OR L4

=> s l2 or l3
L6            62 L2 OR L3

=> s l5 or l6
L7           204 L5 OR L6

=> s l7 and hypertensi?
         79449 HYPERTENSI?
L8           10 L7 AND HYPERTENSI?

=> d l8 1-10 ibib ed abs

L8   ANSWER 1 OF 10  CAPLUS  COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:         2005:120761  CAPLUS
TITLE:                    soluble guanylate cyclase activator and ACE-inhibitor
                          for the treatment of cardiovascular or metabolic
                          disorders
INVENTOR(S):              Fox, David Nathan Abraham; Karran, Eric
                          Howard
PATENT ASSIGNEE(S):       Pfizer Limited, UK; Pfizer Inc.
SOURCE:                   PCT Int. Appl., 27 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.        DATE
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     WO 2005011727         A1    20050210    WO 2004-IB2469         20040726
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
             LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
             NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
             TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
             AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
             EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
             SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
             SN, TD, TG
PRIORITY APPLN. INFO.:                        GB 2003-18094       A  20030801
ED   Entered STN:  11 Feb 2005
AB   The invention discloses combinations comprising (a) an activator of soluble
     guanylate cyclase and (b) an inhibitor of angiotensin converting enzyme
     (ACE) for treating a cardiovascular or metabolic disorder, in particular
     hypertension or diabetes.
REFERENCE COUNT:          10    THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS
                                RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8   ANSWER 2 OF 10  CAPLUS  COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:         2005:101573  CAPLUS
TITLE:                    Hemodynamic effects of phosphodiesterase 5 and
                          angiotensin-converting enzyme inhibition alone or in
                          combination in conscious SHR
```

AUTHOR(S): Gardiner, S. M.; March, J. E.; Kemp, P. A.; Ballard, S. A.; Hawkeswood, E.; **Hughes, B.**; Bennett, T.

CORPORATE SOURCE: Centre for Integrated Systems Biology & Medicine, School of Biomedical Sciences, Queen's Medical Centre, University of Nottingham Medical School, Nottingham, UK

SOURCE: Journal of Pharmacology and Experimental Therapeutics (2005), 312(1), 265-271
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 07 Feb 2005

AB The regional hemodynamic responses to continuous 4-day infusion of UK-357,903 [1-ethyl-4-{3-[3-ethyl-6,7-dihydro-7-oxo-2-(2-pyridylmethyl)-2H-pyrazolo[4,3-d]pyrimidin-5-yl]-2-(2-methoxyethoxy)-5-pyridylsulfonyl}piperazine] (266 μg kg-1 h-1) alone and in combination with a low dose of enalapril (10 μg kg-1 h-1) were measured in conscious spontaneously **hypertensive** rats to test the hypothesis that the renin-angiotensin system may influence the cardiovascular consequences of inhibition of phosphodiesterase 5 (PDE5) by UK-357,903 or vice versa. UK-357,903 alone caused a fall in mean blood pressure (-12.1 mm Hg) associated with vasodilatation in the mesenteric and hindquarters vascular beds. The only way in which the effects of enalapril given alone differed significantly from those of the vehicle was in causing mesenteric vasodilatation, which developed over the 4 days of infusion. UK-357,903 given in combination with enalapril caused hypotension (-17.8 mm Hg) and vasodilatation in the renal, mesenteric, and hindquarter vascular beds. There was evidence of a significant interaction between the effects of the two compds. on renal Doppler shift and vascular conductance with the combined action of the two compds. being greater than the sum of their individual effects. However, although there was a trend for the combination to have greater effects than either of the individual agents on blood pressure and mesenteric vascular conductance, there was no statistical evidence of an interaction. The results indicate that inhibition of the renin-angiotensin system uncovers addnl. renal vasodilator effects of UK-357,903, and/or inhibition of PDE5 enhances the renal vasodilator effects of angiotensin-converting enzyme inhibition.

REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 3 OF 10 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:965255 CAPLUS
DOCUMENT NUMBER: 141:410950

TITLE: Preparation of 5,7-diaminopyrazolo[4,3-d]pyrimidines as selective PDE5 inhibitors useful in the treatment of **hypertension**

INVENTOR(S): Bell, Andrew Simon; Brown, David Graham; **Fox, David Nathan Abraham**; Marsh, Ian Roger; Morrell, Andrew Ian; Palmer, Michael John; Winslow, Carol Ann

PATENT ASSIGNEE(S): Pfizer Limited, UK; Pfizer Inc.

SOURCE: PCT Int. Appl., 279 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004096810	A1	20041111	WO 2004-IB1433	20040422
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,				

CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE,
ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI,
SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN,
TD, TG

NL 1026074	A1	20041101	NL 2004-1026074	20040428
US 2005043325	A1	20050224	US 2004-834484	20040429

PRIORITY APPLN. INFO.:

GB 2003-9780	A	20030429
GB 2003-27748	A	20031128
US 2003-476678P	P	20030606
US 2004-538147P	P	20040120

OTHER SOURCE(S): MARPAT 141:410950
ED Entered STN: 12 Nov 2004
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [wherein R1 = (un)substituted cycloalkyl, cycloalkenyl, (un)substituted pyridin-2-yl, (un)fused Ph, etc.; R2 = H, alkyl; R3, R4 = independently (un)substituted alkyl, alkenyl, cycloalkyl, etc.; or NR3R4 = piperazin-1-yl, monocyclic, saturated polycyclic; R5 = (un)substituted halo/alkyl, alkenyl, alkynyl, cycloalkyl; R6 = H, (un)substituted alkyl, haloalkyl, alkenyl, alkynyl, etc.] were prepared as selective PDE5 inhibitors. For example, II•2HCl was prepared from (4-Methylpyridin-2-yl)amine, dichloride III (general preparation given), and tert-Bu piperazine-1-carboxylate. I gave IC50 values < 10,000 nM in an in vitro assay for PDE5 inhibition. Thus, I are used for treating **hypertension**.
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 4 OF 10 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:152690 CAPLUS
DOCUMENT NUMBER: 140:332158
TITLE: Haemodynamic effects of the selective phosphodiesterase 5 inhibitor, UK-357,903, in conscious SHR
AUTHOR(S): Gardiner, Sheila M.; March, Julie E.; Kemp, Philip A.; Ballard, Stephen A.; Hawkeswood, Ed; **Hughes, Bernadette**; Bennett, Terence
CORPORATE SOURCE: Centre for Integrated Systems Biology & Medicine, School of Biomedical Sciences, Queen's Medical Centre, University of Nottingham Medical School, Nottingham, NG7 2UH, UK
SOURCE: British Journal of Pharmacology (2004), 141(1), 114-122
CODEN: BJPCBM; ISSN: 0007-1188
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 25 Feb 2004
AB 1 Regional haemodynamic responses to a continuous, 4-day infusion of the selective phosphodiesterase type 5 inhibitor, UK-357,903 (0.133 or 1.33 mg kg-1 h-1) were measured in conscious spontaneously **hypertensive** rats, and compared with those of enalapril (1 mg kg-1 h-1). 2 Both doses of UK-357,903 caused modest redns. in mean blood pressure that were not

dose-dependent and only significantly different from the vehicle effects on Day 1 of the study (mean -11.8 and -15.3 mmHg for low and high doses, resp.). UK-357,903 had mesenteric and hindquarters vasodilator effects, which were, again, similar for both dose levels and only significantly different from vehicle on Day 1. Neither dose of UK-357,903 affected renal vascular conductance or heart rate. 3 Although the haemodynamic effects of UK-357,903 were not clearly dose-related and some appeared to wane with time, geometric mean plasma levels of UK-357,903 increased in proportion to dose, and were sustained throughout the infusion period. Furthermore, plasma cGMP, a biomarker of phosphodiesterase 5 inhibition, was persistently elevated, and increased with increasing dose. 4 Enalapril caused a fall in mean blood pressure on day 1 (-14.1 mmHg) that was associated with dilatation in renal, mesenteric and hindquarters vascular beds. The haemodynamic effects of enalapril were sustained or increased over the 4-day infusion, although plasma free drug levels were stable. 5 In conclusion, we have shown regional and temporal changes in the haemodynamic effects of UK-357,903, which may be due to activation of compensatory mechanisms, but there were no signs of functional compensation to the cardiovascular effects of enalapril.

REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 5 OF 10 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:20474 CAPLUS
DOCUMENT NUMBER: 140:71026
TITLE: Novel combination for treating **hypertension**
INVENTOR(S): **Fox, David Nathan Abraham; Hughes, Bernadette**
PATENT ASSIGNEE(S): Pfizer, Limited, UK; Pfizer, Inc.
SOURCE: PCT Int. Appl., 25 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004002461	A2	20040108	WO 2003-IB2657	20030616
WO 2004002461	A3	20040513		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004132731	A1	20040708	US 2003-603369	20030625
PRIORITY APPLN. INFO.:			GB 2002-14784 A	20020626
			US 2002-396780P P	20020717

ED Entered STN: 11 Jan 2004
AB Combinations comprising a) an inhibitor of cyclic guanosine monophosphate (cGMP) specific phosphodiesterase type 5 (PDE5) and b) an angiotensin II receptor antagonist are useful for treating **hypertension**. In the example provided the combined effect in **hypertensive** rats of candesartan and a PDE5 inhibitor was significantly larger than the sum of the 2 individual effects.

L8 ANSWER 6 OF 10 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:950772 CAPLUS
DOCUMENT NUMBER: 140:747

TITLE: Phosphodiesterase 5 inhibitor-ACE inhibitor combination for the treatment of **hypertension**

INVENTOR(S): **Fox, David Nathan Abraham; Hughes, Bernadette**

PATENT ASSIGNEE(S): Pfizer Limited, UK; Pfizer Inc.

SOURCE: PCT Int. Appl., 25 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003099194	A2	20031204	WO 2003-IB1889	20030509
WO 2003099194	A3	20040603		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1506015	A2	20050216	EP 2003-719042	20030509
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US 2004077624	A1	20040422	US 2003-443462	20030522
PRIORITY APPLN. INFO.:			GB 2002-11919 A	20020523
			GB 2002-29784 A	20021220
			US 2002-393418P P	20020702
			US 2003-440206P P	20030114
			WO 2003-IB1889 W	20030509

ED Entered STN: 07 Dec 2003

AB The invention discloses combinations comprising (a) an inhibitor of cyclic guanosine monophosphate (cGMP)-specific phosphodiesterase type 5 (PDE5) inhibitor and (b) an inhibitor of angiotensin converting enzyme (ACE) for treating **hypertension**.

L8 ANSWER 7 OF 10 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:356451 CAPLUS

DOCUMENT NUMBER: 138:368907

TITLE: Preparation of pyrazolo[4,3-d]pyrimidin-7-ones as PDE9 inhibitors for treating cardiovascular disorders

INVENTOR(S): Deninno, Michael Paul; **Hughes, Bernadette**; Kemp, Mark Ian; Palmer, Michael John; Wood, Anthony

PATENT ASSIGNEE(S): Pfizer Limited, UK; Pfizer Inc.

SOURCE: PCT Int. Appl., 69 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003037899	A1	20030508	WO 2002-IB4385	20021022
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,				

UA, UG, US, UZ, VN, YU, ZA, ZM, ZW
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EP 1440073	A1	20040728	EP 2002-777623	20021022
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
BR 2002014096	A	20040928	BR 2002-14096	20021022
US 2003195205	A1	20031016	US 2002-283514	20021030
PRIORITY APPLN. INFO.:			GB 2001-26395 A	20011102
			GB 2001-30695 A	20011221
			GB 2002-16761 A	20020718
			US 2002-350777P P	20020122
			US 2002-399905P P	20020730
			WO 2002-IB4385 W	20021022

OTHER SOURCE(S): MARPAT 138:368907
ED Entered STN: 09 May 2003
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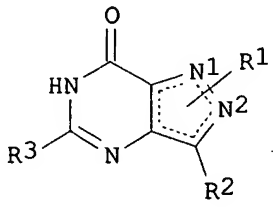

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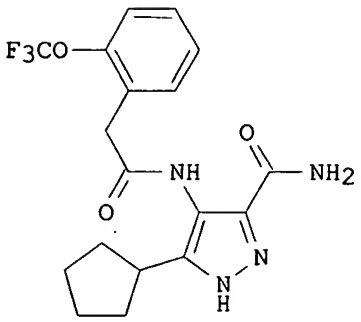

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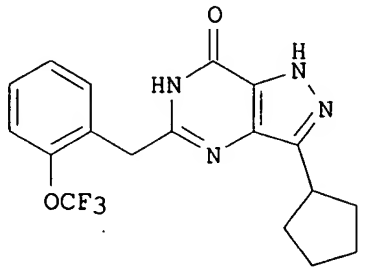


III

AB The title compds. [I; R1 = H, alkyl, wherein R1 is attached to either N1 or N2; R2 = alkyl, hydroxyalkyl, alkoxyalkyl, cycloalkyl, etc.; R3 = alkyl optionally substituted by (un)substituted Ph, cycloalkyl optionally substituted by alkyl, etc.], useful as PDE9 inhibitors for treating cardiovascular disorders, were prepared and formulated. Thus, cyclization of the pyrazolecarboxamide II in the presence of tert-BuOK in iso-PrOH afforded III which was found to have a greater than 40% inhibition against PDE9 at 1 μM.
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 8 OF 10 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1991:241037 CAPLUS
DOCUMENT NUMBER: 114:241037
TITLE: Hemodynamic effects of human α-calcitonin gene-related peptide following administration of endothelin-1 or NG-nitro-L-arginine methyl ester in conscious rats

AUTHOR(S): Gardiner, S. M.; Compton, A. M.; Kemp, P. A.; Bennett, T.; Foulkes, R.; **Hughes, B.**

CORPORATE SOURCE: Med. Sch., Queen's Med. Cent., Nottingham, NG7 2UH, UK

SOURCE: British Journal of Pharmacology (1991), 103(1), 1256-62
CODEN: BJPCBM; ISSN: 0007-1188

DOCUMENT TYPE: Journal

LANGUAGE: English

ED Entered STN: 28 Jun 1991

AB The peripheral hemodynamic effects of human α-calcitonin gene-related peptide (α-CGRP) were studied following administration of endothelin-1 or NG-nitro-L-arginine Me ester (L-NAME), an inhibitor of nitric oxide production, in conscious, chronically-instrumented, Long Evans rats. Infusion of endothelin-1 (3 nmol/kg/h) caused **hypertension**, bradycardia and renal, mesenteric and hindquarters vasoconstrictions. Co-infusion of human α-CGRP (1.5 nmol/kg/h) reduced the **hypertension** and abolished the hindquarters vasoconstriction caused by endothelin-1, but the renal and mesenteric vasoconstrictor actions of endothelin-1 were not affected. Infusion of human α-CGRP (15 nmol/kg/h) in the presence of endothelin-1 caused hypotension and hyperemic vasodilation in the hindquarters; the mesenteric vasoconstrictor effects of endothelin-1 were diminished, but there was only a transient reversal of the renal vasoconstrictor effects of endothelin-1. Pretreatment with the nonpeptide angiotensin II receptor antagonist, DuP 753 (10 mg/kg), caused slight hypotension associated with renal, mesenteric and hindquarters vasodilations, but DuP 753 did not affect responses to endothelin-1 infusion. However, under these conditions coinfusion of human α-CGRP (15 nmol/kg/h) caused a sustained reversal of the renal vasoconstrictor effects of endothelin-1. These results indicate that the failure of human α-CGRP to cause sustained reversal of the renal vasoconstrictor effects of endothelin-1 in the absence of DuP 753 was due to activation of the renin-angiotensin system (possibly as a consequence of the hypotension). In the second experiment, L-NAME (10 mg/kg) caused renal, mesenteric and hindquarters vasoconstrictions similar to those seen in the presence of endothelin-1. However, the renal vasoconstrictor effects of L-NAME were reversed completely by human α-CGRP (15 nmol/kg/h), even though the latter caused hypotension comparable to that seen in the presence of endothelin-1. These results are consistent with a lack of functional activation of the renin-angiotensin system by human α-CGRP in the presence of L-NAME. The vasoconstrictor effects of L-NAME on the hindquarters were completely reversed by infusion of human α-CGRP, but hindquarters flow and vascular conductance did not rise above baseline levels. These results indicate the hindquarters hyperemic vasodilator effects of human α-CGRP seen in the presence of endothelin-1 were contributed to by the nitric oxide-mediated mechanisms.

L8 ANSWER 9 OF 10 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1983:193058 CAPLUS

DOCUMENT NUMBER: 98:193058

TITLE: The release of prostanoids during the acute pulmonary response to E. coli endotoxin in anesthetized cats

AUTHOR(S): Coker, Susan J.; **Hughes, Bernadette**; Parratt, J. R.; Rodger, I. W.; Zeitlin, I. J.

CORPORATE SOURCE: Dep. Physiol. Pharmacol., Univ. Strathclyde, Glasgow, G1 1XW, UK

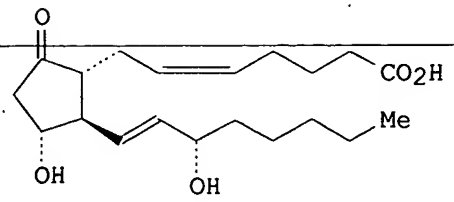
SOURCE: British Journal of Pharmacology (1983), 78(3), 561-70
CODEN: BJPCBM; ISSN: 0007-1188

DOCUMENT TYPE: Journal

LANGUAGE: English

ED Entered STN: 12 May 1984

GI



I

AB The administration of Escherichia coli endotoxin (2 mg/kg, i.v.) to anesthetized cats results in a characteristic acute pulmonary response. This consists of increases in pulmonary artery pressure and airways resistance and a reduction in lung compliance. Plasma concns. of PGE2 (I) [363-24-6], PGF2α [551-11-1], thromboxane B2 [54397-85-2] and 6-keto PGF1α [58962-34-8] were measured by radioimmunoassay in aortic and pulmonary arterial blood samples before, during and after the acute pulmonary response to endotoxin. Endotoxin administration resulted in the rapid release of PGF2α and thromboxane B2 from the lungs. The time course of this release was parallel to that of the pulmonary **hypertensive** and airways responses to endotoxin. PGE2 and 6-keto-PGF1α were released more gradually and with greater variations between individual animals. During the delayed shock phase (2 h after endotoxin) the concns. of PGE2, PGF2α and 6-keto PGF1α were once again elevated in both the aorta and pulmonary artery. Thromboxane B2 concns. were not increased at this time. Thus, PGF2α and thromboxane A2 may be mediators of the acute pulmonary responses to endotoxin.

L8 ANSWER 10 OF 10 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1982:137525 CAPLUS
DOCUMENT NUMBER: 96:137525
TITLE: Polymyxin B sulfate protects cats against the hemodynamic and metabolic effects of E. coli endotoxin
AUTHOR(S): **Hughes, Bernadette**; Madan, B. R.; Parratt, J. R.
CORPORATE SOURCE: Dep. Physiol. Pharmacol., Univ. Strathclyde, Glasgow, G1 1XW, UK
SOURCE: British Journal of Pharmacology (1981), 74(3), 701-7
CODEN: BJPCBM; ISSN: 0007-1188
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 12 May 1984
AB polymyxin B sulfate (I) [1405-20-5] given i.v. 1 min before Escherichia coli endotoxin (2 mg/kg, i.v.) as a bolus injection (5 mg/kg) followed by a continuous i.v. infusion (addnl. 5 mg/kg given over a 30 min period) prevented the endotoxin-induced pulmonary (right atrial) **hypertension** but not the acute systemic **hypertension** in anesthetized cats. I reduced the delayed hemodynamic effects of endotoxin (systemic hypotension, decrease in cardiac output), but did not prevent the initial (1-3 h) and marked metabolic acidosis, although after 3 h arterial lactate levels returned towards control levels, whereas in the endotoxin-only group they continued to increase until death. The mechanism of this marked protective effect and the possible clin. repercussions are discussed; the most likely explanation for the protection is in chemical combination with the lipid A moiety of the endotoxin.

=> d his

(FILE 'HOME' ENTERED AT 11:49:08 ON 02 MAR 2005)

FILE 'CAPLUS' ENTERED AT 11:49:13 ON 02 MAR 2005

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                E FOX DAVID/AU
L1           69 S E2-E3, E20-E22
                E HUGHES BERNADETTE/AU
L2           22 S E3-E4
                E HUGHES B/AU
L3           40 S E3
                E FOX D/AU
                E FOX D?/AU
                E FOX D/AU
L4           75 S E3
L5          144 S L1 OR L4
L6           62 S L2 OR L3
L7          204 S L5 OR L6
L8           10 S L7 AND HYPERTENSI?

=> s l7 and (cyclic guanosine monophosphate (w) (phosphodiesterase or "PDE5")) and
(angiotensin)
        286246 CYCLIC
            330 CYCLICS
        286374 CYCLIC
                  (CYCLIC OR CYCLICS)
         21456 GUANOSINE
           313 GUANOSINES
         21565 GUANOSINE
                  (GUANOSINE OR GUANOSINES)
         29181 MONOPHOSPHATE
          3848 MONOPHOSPHATES
         31896 MONOPHOSPHATE
                  (MONOPHOSPHATE OR MONOPHOSPHATES)
           835 CYCLIC GUANOSINE MONOPHOSPHATE
                  (CYCLIC(W)GUANOSINE(W)MONOPHOSPHATE)
         24057 PHOSPHODIESTERASE
          2560 PHOSPHODIESTERASES
         24563 PHOSPHODIESTERASE
                  (PHOSPHODIESTERASE OR PHOSPHODIESTERASES)
           533 "PDE5"
            35 CYCLIC GUANOSINE MONOPHOSPHATE (W) (PHOSPHODIESTERASE OR "PDE5")
         54762 ANGIOTENSIN
          1691 ANGIOTENSINS
         54850 ANGIOTENSIN
                  (ANGIOTENSIN OR ANGIOTENSINS)
L9           0 L7 AND (CYCLIC GUANOSINE MONOPHOSPHATE (W) (PHOSPHODIESTERASE
                  OR "PDE5")) AND (ANGIOTENSIN)

=> s l7 and ("cgmp" or "pde5" or "angiotensin II receptor antagonist")
         20057 "CGMP"
           187 "CGMPS"
         20081 "CGMP"
                  ("CGMP" OR "CGMPS")
           533 "PDE5"
         54762 "ANGIOTENSIN"
          1691 "ANGIOTENSINS"
         54850 "ANGIOTENSIN"
                  ("ANGIOTENSIN" OR "ANGIOTENSINS")
       2015064 "II"
           825 "IIS"
       2015534 "II"
                  ("II" OR "IIS")
        591069 "RECEPTOR"
        542204 "RECEPTORS"
        703691 "RECEPTOR"
                  ("RECEPTOR" OR "RECEPTORS")
        149224 "ANTAGONIST"
        108335 "ANTAGONISTS"
```

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        200876 "ANTAGONIST"
                ("ANTAGONIST" OR "ANTAGONISTS")
          1675 "ANGIOTENSIN II RECEPTOR ANTAGONIST"
                ("ANGIOTENSIN"(W)"II"(W)"RECEPTOR"(W)"ANTAGONIST")
L10            6 L7 AND ("CGMP" OR "PDE5" OR "ANGIOTENSIN II RECEPTOR ANTAGONIST"
                )

=> d l10 1-6 ibib ed abs

L10  ANSWER 1 OF 6  CAPLUS  COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:         2005:101573  CAPLUS
TITLE:                    Hemodynamic effects of phosphodiesterase 5 and
                          angiotensin-converting enzyme inhibition alone or in
                          combination in conscious SHR
AUTHOR(S):                Gardiner, S. M.; March, J. E.; Kemp, P. A.; Ballard,
                          S. A.; Hawkeswood, E.; Hughes, B.; Bennett,
                          T.
CORPORATE SOURCE:         Centre for Integrated Systems Biology & Medicine,
                          School of Biomedical Sciences, Queen's Medical Centre,
                          University of Nottingham Medical School, Nottingham,
                          UK
SOURCE:                   Journal of Pharmacology and Experimental Therapeutics
                          (2005), 312(1), 265-271
                          CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER:                American Society for Pharmacology and Experimental
                          Therapeutics
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
ED   Entered STN:  07 Feb 2005
AB   The regional hemodynamic responses to continuous 4-day infusion of
     UK-357,903 [1-ethyl-4-{3-[3-ethyl-6,7-dihydro-7-oxo-2-(2-pyridylmethyl)-2H-
     pyrazolo[4,3-d]pyrimidin-5-yl]-2-(2-methoxyethoxy)-5-
     pyridylsulfonyl}piperazine] (266 μg kg-1 h-1) alone and in combination
     with a low dose of enalapril (10 μg kg-1 h-1) were measured in
     conscious spontaneously hypertensive rats to test the hypothesis that the
     renin-angiotensin system may influence the cardiovascular consequences of
     inhibition of phosphodiesterase 5 (PDE5) by UK-357,903 or vice
     versa.  UK-357,903 alone caused a fall in mean blood pressure (-12.1 mm
     Hg) associated with vasodilatation in the mesenteric and hindquarters
     vascular beds.  The only way in which the effects of enalapril given alone
     differed significantly from those of the vehicle was in causing mesenteric
     vasodilatation, which developed over the 4 days of infusion.  UK-357,903
     given in combination with enalapril caused hypotension (-17.8 mm Hg) and
     vasodilatation in the renal, mesenteric, and hindquarter vascular beds.
     There was evidence of a significant interaction between the effects of the
     two compds. on renal Doppler shift and vascular conductance with the
     combined action of the two compds. being greater than the sum of their
     individual effects.  However, although there was a trend for the
     combination to have greater effects than either of the individual agents
     on blood pressure and mesenteric vascular conductance, there was no
     statistical evidence of an interaction.  The results indicate that
     inhibition of the renin-angiotensin system uncovers addnl. renal
     vasodilator effects of UK-357,903, and/or inhibition of PDE5
     enhances the renal vasodilator effects of angiotensin-converting enzyme
     inhibition.
REFERENCE COUNT:          15    THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS
                                RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10  ANSWER 2 OF 6  CAPLUS  COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:         2004:965255  CAPLUS
DOCUMENT NUMBER:          141:410950
TITLE:                    Preparation of 5,7-diaminopyrazolo[4,3-d]pyrimidines
                          as selective PDE5 inhibitors useful in the
                          treatment of hypertension
```

INVENTOR(S): Bell, Andrew Simon; Brown, David Graham; **Fox, David Nathan Abraham**; Marsh, Ian Roger; Morrell, Andrew Ian; Palmer, Michael John; Winslow, Carol Ann

PATENT ASSIGNEE(S): Pfizer Limited, UK; Pfizer Inc.

SOURCE: PCT Int. Appl., 279 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004096810	A1	20041111	WO 2004-IB1433	20040422
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
NL 1026074	A1	20041101	NL 2004-1026074	20040428
US 2005043325	A1	20050224	US 2004-834484	20040429

PRIORITY APPLN. INFO.:		
GB 2003-9780	A	20030429
GB 2003-27748	A	20031128
US 2003-476678P	P	20030606
US 2004-538147P	P	20040120

OTHER SOURCE(S): MARPAT 141:410950

ED Entered STN: 12 Nov 2004

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [wherein R1 = (un)substituted cycloalkyl, cycloalkenyl, (un)substituted pyridin-2-yl, (un)fused Ph, etc.; R2 = H, alkyl; R3, R4 = independently (un)substituted alkyl, alkenyl, cycloalkyl, etc.; or NR3R4 = piperazin-1-yl, monocyclic, saturated polycyclic; R5 = (un)substituted halo/alkyl, alkenyl, alkynyl, cycloalkyl; R6 = H, (un)substituted alkyl, haloalkyl, alkenyl, alkynyl, etc.] were prepared as selective **PDE5** inhibitors. For example, II•2HCl was prepared from (4-Methylpyridin-2-yl)amine, dichloride III (general preparation given), and tert-Bu piperazine-1-carboxylate. I gave IC50 values < 10,000 nM in an in vitro assay for **PDE5** inhibition. Thus, I are used for treating hypertension.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:152690 CAPLUS

DOCUMENT NUMBER: 140:332158

TITLE: Haemodynamic effects of the selective phosphodiesterase 5 inhibitor, UK-357,903, in conscious SHR

AUTHOR(S): Gardiner, Sheila M.; March, Julie E.; Kemp, Philip A.; Ballard, Stephen A.; Hawkeswood, Ed; **Hughes, Bernadette**; Bennett, Terence

CORPORATE SOURCE: Centre for Integrated Systems Biology & Medicine,

School of Biomedical Sciences, Queen's Medical Centre, University of Nottingham Medical School, Nottingham, NG7 2UH, UK

SOURCE: British Journal of Pharmacology (2004), 141(1), 114-122
CODEN: BJPCBM; ISSN: 0007-1188

PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 25 Feb 2004

AB 1 Regional haemodynamic responses to a continuous, 4-day infusion of the selective phosphodiesterase type 5 inhibitor, UK-357,903 (0.133 or 1.33 mg kg-1 h-1) were measured in conscious spontaneously hypertensive rats, and compared with those of enalapril (1 mg kg-1 h-1). 2 Both doses of UK-357,903 caused modest redns. in mean blood pressure that were not dose-dependent and only significantly different from the vehicle effects on Day 1 of the study (mean -11.8 and -15.3 mmHg for low and high doses, resp.). UK-357,903 had mesenteric and hindquarters vasodilator effects, which were, again, similar for both dose levels and only significantly different from vehicle on Day 1. Neither dose of UK-357,903 affected renal vascular conductance or heart rate. 3 Although the haemodynamic effects of UK-357,903 were not clearly dose-related and some appeared to wane with time, geometric mean plasma levels of UK-357,903 increased in proportion to dose, and were sustained throughout the infusion period. Furthermore, plasma **cGMP**, a biomarker of phosphodiesterase 5 inhibition, was persistently elevated, and increased with increasing dose. 4 Enalapril caused a fall in mean blood pressure on day 1 (-14.1 mmHg) that was associated with dilatation in renal, mesenteric and hindquarters vascular beds. The haemodynamic effects of enalapril were sustained or increased over the 4-day infusion, although plasma free drug levels were stable. 5 In conclusion, we have shown regional and temporal changes in the haemodynamic effects of UK-357,903, which may be due to activation of compensatory mechanisms, but there were no signs of functional compensation to the cardiovascular effects of enalapril.

REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:20474 CAPLUS
DOCUMENT NUMBER: 140:71026
TITLE: Novel combination for treating hypertension
INVENTOR(S): **Fox, David Nathan Abraham; Hughes, Bernadette**
PATENT ASSIGNEE(S): Pfizer, Limited, UK; Pfizer, Inc.
SOURCE: PCT Int. Appl., 25 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004002461	A2	20040108	WO 2003-IB2657	20030616
WO 2004002461	A3	20040513		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,

BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2004132731	A1	20040708	US 2003-603369		20030625
PRIORITY APPLN. INFO.:			GB 2002-14784	A	20020626
			US 2002-396780P	P	20020717

ED Entered STN: 11 Jan 2004

AB Combinations comprising a) an inhibitor of cyclic guanosine monophosphate (**cGMP**) specific phosphodiesterase type 5 (**PDE5**) and b) an **angiotensin II receptor antagonist** are useful for treating hypertension. In the example provided the combined effect in hypertensive rats of candesartan and a **PDE5** inhibitor was significantly larger than the sum of the 2 individual effects.

L10 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:950772 CAPLUS
DOCUMENT NUMBER: 140:747
TITLE: Phosphodiesterase 5 inhibitor-ACE inhibitor combination for the treatment of hypertension
INVENTOR(S): **Fox, David Nathan Abraham; Hughes, Bernadette**
PATENT ASSIGNEE(S): Pfizer Limited, UK; Pfizer Inc.
SOURCE: PCT Int. Appl., 25 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003099194	A2	20031204	WO 2003-IB1889	20030509
WO 2003099194	A3	20040603		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1506015	A2	20050216	EP 2003-719042	20030509
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
US 2004077624	A1	20040422	US 2003-443462	20030522
PRIORITY APPLN. INFO.:			GB 2002-11919	A 20020523
			GB 2002-29784	A 20021220
			US 2002-393418P	P 20020702
			US 2003-440206P	P 20030114
			WO 2003-IB1889	W 20030509

ED Entered STN: 07 Dec 2003

AB The invention discloses combinations comprising (a) an inhibitor of cyclic guanosine monophosphate (**cGMP**)-specific phosphodiesterase type 5 (**PDE5**) inhibitor and (b) an inhibitor of angiotensin converting enzyme (ACE) for treating hypertension.

L10 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1991:241037 CAPLUS
DOCUMENT NUMBER: 114:241037
TITLE: Hemodynamic effects of human α-calcitonin gene-related peptide following administration of endothelin-1 or NG-nitro-L-arginine methyl ester in conscious rats

AUTHOR(S): Gardiner, S. M.; Compton, A. M.; Kemp, P. A.; Bennett, T.; Foulkes, R.; **Hughes, B.**

CORPORATE SOURCE: Med. Sch., Queen's Med. Cent., Nottingham, NG7 2UH, UK

SOURCE: British Journal of Pharmacology (1991), 103(1), 1256-62
CODEN: BJPCBM; ISSN: 0007-1188

DOCUMENT TYPE: Journal

LANGUAGE: English

ED Entered STN: 28 Jun 1991

AB The peripheral hemodynamic effects of human α-calcitonin gene-related peptide (α-CGRP) were studied following administration of endothelin-1 or NG-nitro-L-arginine Me ester (L-NAME), an inhibitor of nitric oxide production, in conscious, chronically-instrumented, Long Evans rats. Infusion of endothelin-1 (3 nmol/kg/h) caused hypertension, bradycardia and renal, mesenteric and hindquarters vasoconstrictions. Co-infusion of human α-CGRP (1.5 nmol/kg/h) reduced the hypertension and abolished the hindquarters vasoconstriction caused by endothelin-1, but the renal and mesenteric vasoconstrictor actions of endothelin-1 were not affected. Infusion of human α-CGRP (15 nmol/kg/h) in the presence of endothelin-1 caused hypotension and hyperemic vasodilation in the hindquarters; the mesenteric vasoconstrictor effects of endothelin-1 were diminished, but there was only a transient reversal of the renal vasoconstrictor effects of endothelin-1. Pretreatment with the nonpeptide **angiotensin II receptor antagonist**, DuP 753 (10 mg/kg), caused slight hypotension associated with renal, mesenteric and hindquarters vasodilations, but DuP 753 did not affect responses to endothelin-1 infusion. However, under these conditions coinfusion of human α-CGRP (15 nmol/kg/h) caused a sustained reversal of the renal vasoconstrictor effects of endothelin-1. These results indicate that the failure of human α-CGRP to cause sustained reversal of the renal vasoconstrictor effects of endothelin-1 in the absence of DuP 753 was due to activation of the renin-angiotensin system (possibly as a consequence of the hypotension). In the second experiment, L-NAME (10 mg/kg) caused renal, mesenteric and hindquarters vasoconstrictions similar to those seen in the presence of endothelin-1. However, the renal vasoconstrictor effects of L-NAME were reversed completely by human α-CGRP (15 nmol/kg/h), even though the latter caused hypotension comparable to that seen in the presence of endothelin-1. These results are consistent with a lack of functional activation of the renin-angiotensin system by human α-CGRP in the presence of L-NAME. The vasoconstrictor effects of L-NAME on the hindquarters were completely reversed by infusion of human α-CGRP, but hindquarters flow and vascular conductance did not rise above baseline levels. These results indicate the hindquarters hyperemic vasodilator effects of human α-CGRP seen in the presence of endothelin-1 were contributed to by the nitric oxide-mediated mechanisms.

=> d cost

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
CONNECT CHARGES	5.46	5.61
NETWORK CHARGES	0.84	0.90
SEARCH CHARGES	41.58	41.58
DISPLAY CHARGES	42.40	42.40
FULL ESTIMATED COST	90.28	90.49

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-11.68	-11.68

IN FILE 'CAPLUS' AT 11:57:36 ON 02 MAR 2005

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=> d his

     (FILE 'HOME' ENTERED AT 11:49:08 ON 02 MAR 2005)

     FILE 'CAPLUS' ENTERED AT 11:49:13 ON 02 MAR 2005
                E FOX DAVID/AU
L1           69 S E2-E3, E20-E22
                E HUGHES BERNADETTE/AU
L2           22 S E3-E4
                E HUGHES B/AU
L3           40 S E3
                E FOX D/AU
                E FOX D?/AU
                E FOX D/AU
L4           75 S E3
L5          144 S L1 OR L4
L6           62 S L2 OR L3
L7          204 S L5 OR L6
L8           10 S L7 AND HYPERTENSI?
L9            0 S L7 AND (CYCLIC GUANOSINE MONOPHOSPHATE (W) (PHOSPHODIESTERASE
L10           6 S L7 AND ("CGMP" OR "PDE5" OR "ANGIOTENSIN II RECEPTOR ANTAGONI

=> file registry
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                    90.28      90.49

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                       ENTRY    SESSION
CA SUBSCRIBER PRICE                                   -11.68     -11.68

FILE 'REGISTRY' ENTERED AT 11:57:43 ON 02 MAR 2005
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DICTIONARY FILE UPDATES:   1 MAR 2005  HIGHEST RN 840454-17-3

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 18, 2005

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=> e sildenafil/cn
E1            1     SILD (STREPTOCOCCUS PYOGENES GENE SILD)/CN
E2            1     SILDATE/CN
E3            1 --> SILDENAFIL/CN
E4            1     SILDENAFIL CITRATE/CN
E5            1     SILDENAFIL MALEATE/CN
E6            1     SILDENAFIL MONOMALEATE/CN
E7            1     SILDENAFIL NITRATE/CN
E8            1     SILDEX/CN
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E9            1     SILDEX C 303/CN
E10           1     SILDEX H 121/CN
E11           1     SILDEX H 32/CN
E12           1     SILDEX H 51/CN

=> s e3-e4
              1 SILDENAFIL/CN
              1 "SILDENAFIL CITRATE"/CN
L11           2 (SILDENAFIL/CN OR "SILDENAFIL CITRATE"/CN)

=> e tadalafil/an
'AN' IS NOT A VALID EXPAND FIELD CODE FOR FILE 'REGISTRY'
The indicated field code is not available for EXPAND in this
file.  To see a list of valid EXPAND field codes, enter HELP
SFIELDS at an arrow prompt (=>).

=> e tadalafil/cn
E1            1     TADA3L PROTEIN (MOUSE STRAIN FVB/N CLONE MGC:31487 IMAGE:448
                    6171)/CN
E2            1     TADAB/CN
E3            1 --> TADALAFIL/CN
E4            1     TADB/CN
E5            1     TADB (PASTEURELLA MULTOCIDA STRAIN IL1403 CLONE PM70 GENE TA
                    DB)/CN
E6            1     TADB (VIBRIO PARAHAEMOLYTICUS STRAIN O3:K6 GENE VPA0725)/CN
E7            1     TADB PROTEIN (CHLOROBIUM TEPIDUM STRAIN TLS GENE TADB)/CN
E8            1     TADB-LIKE PROTEIN (PLASMID PBD2 GENE PBD2.017)/CN
E9            1     TADC (PASTEURELLA MULTOCIDA STRAIN IL1403 CLONE PM70 GENE TA
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E10           1     TADC (VIBRIO PARAHAEMOLYTICUS STRAIN O3:K6 GENE VPA0726)/CN
E11           1     TADC PROTEIN (CHLOROBIUM TEPIDUM STRAIN TLS GENE CT0436)/CN
E12           1     TADCO ALPHA BLUE DYE/CN

=> s e3
L12           1 TADALAFIL/CN

=> e vardenafil/cn
E1            1     VARD/CN
E2            1     VARDAX/CN
E3            1 --> VARDENAFIL/CN
E4            1     VARDENAFIL DIHYDROCHLORIDE/CN
E5            1     VARDENAFIL HYDROCHLORIDE/CN
E6            1     VARDHAK/CN
E7            1     VARDHMAN/CN
E8            1     VAREBIAN/CN
E9            1     VARENICLINE/CN
E10           1     VARENICLINE TARTRATE/CN
E11           1     VARENNESITE/CN
E12           1     VARENNESITE ((MN0.5-1FE0-0.5)2NA8((OH)0.5-1CL0-0.5)2(SI2O5)5
                    .12H2O)/CN

=> s e3-e5
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              1 "VARDENAFIL DIHYDROCHLORIDE"/CN
              1 "VARDENAFIL HYDROCHLORIDE"/CN
L13           3 (VARDENAFIL/CN OR "VARDENAFIL DIHYDROCHLORIDE"/CN OR "VARDENAFIL
                 HYDROCHLORIDE"/CN)

=> s candesartan/cn
L14           1 CANDESARTAN/CN

=> e candesartan/cn
E1            1     CANDESALVONE B METHYL ESTER/CN
E2            1     CANDESALVOQUINONE/CN
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E3            1 --> CANDESARTAN/CN
E4            1     CANDESARTAN CILEXETIL/CN
E5            1     CANDESARTAN M1/CN
E6            1     CANDEX/CN
E7            1     CANDICANDIOL/CN
E8            1     CANDICANDIOL A/CN
E9            1     CANDICANDIOL B/CN
E10           1     CANDICANDIOL DIACETATE/CN
E11           1     CANDICANIN/CN
E12           1     CANDICANIN ACETATE/CN

=> s e3-e5
              1 CANDESARTAN/CN
              1 "CANDESARTAN CILEXETIL"/CN
              1 "CANDESARTAN M1"/CN
L15           2 (CANDESARTAN/CN OR "CANDESARTAN CILEXETIL"/CN OR "CANDESARTAN
                M1"/CN)

=> e eprosartan/cn
E1            1     EPROLIN S/CN
E2            1     EPRONAZ/CN
E3            1 --> EPROSARTAN/CN
E4            1     EPROSARTAN MESYLATE/CN
E5            1     EPROSARTAN METHANESULFONATE/CN
E6            1     EPROSIN/CN
E7            1     EPROSIN 15/CN
E8            1     EPROSIN E 1/CN
E9            1     EPROSIN E 26/CN
E10           1     EPROSIN E 3/CN
E11           1     EPROSIN T 05/CN
E12           1     EPROSIN T 06/CN

=> s e3-e5
              1 EPROSARTAN/CN
              1 "EPROSARTAN MESYLATE"/CN
              1 "EPROSARTAN METHANESULFONATE"/CN
L16           2 (EPROSARTAN/CN OR "EPROSARTAN MESYLATE"/CN OR "EPROSARTAN METHAN
                ESULFONATE"/CN)

=> e irbesartan/cn
E1            1     IRB5 (VIBRIO CHOLERAE STRAIN 569B CLONE PRAP5 )/CN
E2            1     IRBADAZINE/CN
E3            1 --> IRBESARTAN/CN
E4            1     IRBESARTAN METABOLITE 5/CN
E5            1     IRBESARTAN METABOLITE 7/CN
E6            1     IRBESARTAN-HYDROCHLOROTHIAZIDE MIXT./CN
E7            1     IRBP (ALLENOPITHECUS NIGROVIRIDIS STRAIN SPECIMEN-VOUCHER-R1
                    46/97 GENE IRBP FRAGMENT)/CN
E8            1     IRBP (CERCOPITHECUS MONA STRAIN COUNTRY-GRENADA-SPECIMEN-VOU
                    CHER-SA.BF#3 GENE IRBP FRAGMENT)/CN
E9            1     IRBP (INTERSTITIAL RETINOL-BINDING PROTEIN) (DROSOPHILA MELA
                    NOGASTER)/CN
E10           1     IRBP (MACACA ARCTOIDES STRAIN COUNTRY-MALAYSIA-SPECIMEN-VOUC
                    HER-101.MALAYA GENE IRBP FRAGMENT)/CN
E11           1     IRBP (MACACA ARCTOIDES STRAIN COUNTRY-VIET-NAM-SPECIMEN-VOUC
                    HER-HANOI.05.2 GENE IRBP FRAGMENT)/CN
E12           1     IRBP (MACACA ARCTOIDES STRAIN SPECIMEN-VOUCHER-ST0316 GENE I
                    RBP FRAGMENT)/CN

=> s e3-e6
              1 IRBESARTAN/CN
              1 "IRBESARTAN METABOLITE 5"/CN
              1 "IRBESARTAN METABOLITE 7"/CN
              1 "IRBESARTAN-HYDROCHLOROTHIAZIDE MIXT."/CN
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L17           4 (IRBESARTAN/CN OR "IRBESARTAN METABOLITE 5"/CN OR "IRBESARTAN
                METABOLITE 7"/CN OR "IRBESARTAN-HYDROCHLOROTHIAZIDE MIXT."/CN)
```

```
=> e losartan/cn
E1            1      LOSAN/CN
E2            1      LOSANTIN/CN
E3            1 --> LOSARTAN/CN
E4            1      LOSARTAN MONOPOTASSIUM SALT/CN
E5            1      LOSARTAN P-TOLUENESULFONATE/CN
E6            1      LOSARTAN POTASSIUM/CN
E7            1      LOSARTAN-HYDROCHLOROTHIAZIDE MIXT./CN
E8            1      LOSBANINE/CN
E9            1      LOSE-URONATE KETOL-ISOMERASE (YERSINIA PESTIS STRAIN CO92 GE
                     NE KDUI)/CN
E10           1      LOSEC/CN
E11           1      LOSEC SODIUM/CN
E12           1      LOSEYITE/CN

=> s e3-e7
              1 LOSARTAN/CN
              1 "LOSARTAN MONOPOTASSIUM SALT"/CN
              1 "LOSARTAN P-TOLUENESULFONATE"/CN
              1 "LOSARTAN POTASSIUM"/CN
              1 "LOSARTAN-HYDROCHLOROTHIAZIDE MIXT."/CN
L18           4 (LOSARTAN/CN OR "LOSARTAN MONOPOTASSIUM SALT"/CN OR "LOSARTAN
                P-TOLUENESULFONATE"/CN OR "LOSARTAN POTASSIUM"/CN OR "LOSARTAN-H
                YDROCHLOROTHIAZIDE MIXT."/CN)

=> e olmesartan/cn
E1            1      OLMECOL/CN
E2            1      OLMELIN/CN
E3            1 --> OLMESARTAN/CN
E4            1      OLMESARTAN MEDOXOMIL/CN
E5            1      OLMETEC/CN
E6            1      OLMIDE/CN
E7            1      OLMIDINE/CN
E8            1      OLMIFON/CN
E9            1      OLMSTEADITE/CN
E10           1      OLN 4/CN
E11           1      OLN 50/CN
E12           1      OLN-1/CN

=> s e3-e5
              1 OLMESARTAN/CN
              1 "OLMESARTAN MEDOXOMIL"/CN
              1 OLMETEC/CN
L19           2 (OLMESARTAN/CN OR "OLMESARTAN MEDOXOMIL"/CN OR OLMETEC/CN)

=> e saralasin/cn
E1            1      SARAINE C ACETATE/CN
E2            1      SARAKALIM/CN
E3            1 --> SARALASIN/CN
E4            1      SARALASIN ACETATE/CN
E5            1      SARALINE 200/CN
E6            1      SARALINK 545/CN
E7            1      SARAMET/CN
E8            1      SARAMIN/CN
E9            1      SARAMYCETIC ACID/CN
E10           1      SARAMYCETIC ACID A/CN
E11           1      SARAMYCETIN/CN
E12           1      SARAMYCETOIC ACID/CN

=> s e3-e4
              1 SARALASIN/CN
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```
             1 "SARALASIN ACETATE"/CN
L20          2 (SARALASIN/CN OR "SARALASIN ACETATE"/CN)
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```
=> e telmisartan/cn
E1           1     TELMIN B/CN
E2           1     TELMION/CN
E3           1 --> TELMISARTAN/CN
E4           1     TELMISARTAN GLUCURONIDE/CN
E5           1     TELMISARTAN HYDROCHLORIDE/CN
E6           1     TELMISARTAN SODIUM HEMIHYDRATE/CN
E7           1     TELMISARTAN SODIUM SALT/CN
E8           1     TELO-PROPEPTIDE OF ALPHA 1 (III) PROCOLLAGEN (HUMAN)/CN
E9           1     TELOBINE/CN
E10          1     TELOCINOBUFAGIN/CN
E11          1     TELOCINOBUFAGIN 3-HEMISUBERATE/CN
E12          1     TELOCINOBUFAGIN 3-HEMISUBERATE P-NITROPHENYL ESTER/CN

=> s e3-e7
             1 TELMISARTAN/CN
             1 "TELMISARTAN GLUCURONIDE"/CN
             1 "TELMISARTAN HYDROCHLORIDE"/CN
             1 "TELMISARTAN SODIUM HEMIHYDRATE"/CN
             1 "TELMISARTAN SODIUM SALT"/CN
L21          5 (TELMISARTAN/CN OR "TELMISARTAN GLUCURONIDE"/CN OR "TELMISARTAN
               HYDROCHLORIDE"/CN OR "TELMISARTAN SODIUM HEMIHYDRATE"/CN OR
               "TELMISARTAN SODIUM SALT"/CN)

=> e valsartan/cn
E1           1     VALSARIN/CN
E2           1     VALSARIN ACETATE/CN
E3           1 --> VALSARTAN/CN
E4           1     VALSARTAN METHYL ESTER/CN
E5           1     VALSOF PE 40/CN
E6           1     VALSOL LTA/CN
E7           1     VALSOL LTA-N/CN
E8           1     VALSPAR/CN
E9           1     VALSPAR EPS 2718/CN
E10          1     VALSPAR FBE-D 2003DV/CN
E11          1     VALSPAR S 9783-002/CN
E12          1     VALSPEX 155-53/CN

=> s e3-e4
             1 VALSARTAN/CN
             1 "VALSARTAN METHYL ESTER"/CN
L22          2 (VALSARTAN/CN OR "VALSARTAN METHYL ESTER"/CN)

=> d his

     (FILE 'HOME' ENTERED AT 11:49:08 ON 02 MAR 2005)

     FILE 'CAPLUS' ENTERED AT 11:49:13 ON 02 MAR 2005
                E FOX DAVID/AU
L1          69 S E2-E3, E20-E22
                E HUGHES BERNADETTE/AU
L2          22 S E3-E4
                E HUGHES B/AU
L3          40 S E3
                E FOX D/AU
                E FOX D?/AU
                E FOX D/AU
L4          75 S E3
L5         144 S L1 OR L4
L6          62 S L2 OR L3
L7         204 S L5 OR L6
```

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L8            10 S L7 AND HYPERTENSI?
L9             0 S L7 AND (CYCLIC GUANOSINE MONOPHOSPHATE (W) (PHOSPHODIESTERASE
L10            6 S L7 AND ("CGMP" OR "PDE5" OR "ANGIOTENSIN II RECEPTOR ANTAGONI

     FILE 'REGISTRY' ENTERED AT 11:57:43 ON 02 MAR 2005
                  E SILDENAFIL/CN
L11            2 S E3-E4
                  E TADALAFIL/CN
L12            1 S E3
                  E VARDENAFIL/CN
L13            3 S E3-E5
L14            1 S CANDESARTAN/CN
                  E CANDESARTAN/CN
L15            2 S E3-E5
                  E EPROSARTAN/CN
L16            2 S E3-E5
                  E IRBESARTAN/CN
L17            4 S E3-E6
                  E LOSARTAN/CN
L18            4 S E3-E7
                  E OLMESARTAN/CN
L19            2 S E3-E5
                  E SARALASIN/CN
L20            2 S E3-E4
                  E TELMISARTAN/CN
L21            5 S E3-E7
                  E VALSARTAN/CN
L22            2 S E3-E4

=> d cost
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
CONNECT CHARGES                                         1.85       7.46
NETWORK CHARGES                                         0.30       1.20
SEARCH CHARGES                                        156.40     197.98
DISPLAY CHARGES                                         0.00      42.40
                                                      -------    -------
FULL ESTIMATED COST                                   158.55     249.04

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                       ENTRY    SESSION
CA SUBSCRIBER PRICE                                     0.00     -11.68

IN FILE 'REGISTRY' AT 12:00:50 ON 02 MAR 2005


=> s l11 or l12 or l13
L23            6 L11 OR L12 OR L13

=> s l15 or l16 or l17 or l18 or l19 or l20 or l21 or l22
L24           23 L15 OR L16 OR L17 OR L18 OR L19 OR L20 OR L21 OR L22

=> file caplus
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                   159.41     249.90

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                       ENTRY    SESSION
CA SUBSCRIBER PRICE                                     0.00     -11.68

FILE 'CAPLUS' ENTERED AT 12:02:01 ON 02 MAR 2005
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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FILE COVERS 1907 - 2 Mar 2005 VOL 142 ISS 10
FILE LAST UPDATED: 1 Mar 2005 (20050301/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

```
=> s l23
L25        1081 L23

=> s l24
L26        4320 L24

=> e hypertension/bi
E1            2     HYPERTENSIO/BI
E2            3     HYPERTENSIOGENIC/BI
E3        70452 --> HYPERTENSION/BI
E4            1     HYPERTENSION1/BI
E5            1     HYPERTENSION3/BI
E6            2     HYPERTENSION5/BI
E7            3     HYPERTENSIONAL/BI
E8            1     HYPERTENSIONC/BI
E9            1     HYPERTENSIONGENIC/BI
E10           1     HYPERTENSIONN/BI
E11           1     HYPERTENSIONOGENIC/BI
E12           1     HYPERTENSIONOLOGY/BI

=> e
E13          96     HYPERTENSIONS/BI
E14           1     HYPERTENSISVE/BI
E15           1     HYPERTENSIV/BI
E16       34458     HYPERTENSIVE/BI
E17           4     HYPERTENSIVELY/BI
E18           1     HYPERTENSIVEN/BI
E19           1     HYPERTENSIVENESS/BI
E20           1     HYPERTENSIVERATS/BI
E21        1927     HYPERTENSIVES/BI
E22           1     HYPERTENSIVEW/BI
E23           1     HYPERTENSIVITY/BI
E24           9     HYPERTENSOGENIC/BI

=> s e3, e16
          70452 HYPERTENSION/BI
             96 HYPERTENSIONS/BI
          70470 HYPERTENSION/BI
                  ((HYPERTENSION OR HYPERTENSIONS)/BI)
          34458 HYPERTENSIVE/BI
           1927 HYPERTENSIVES/BI
          35172 HYPERTENSIVE/BI
                  ((HYPERTENSIVE OR HYPERTENSIVES)/BI)
L27       78751 (HYPERTENSION/BI OR  HYPERTENSIVE/BI)
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=> e hypertension/ct
E#    FREQUENCY     AT      TERM
--    ---------     --      ----
E1            1      7      HYPERTELIS/CT
E2            0     10      HYPERTENSIN/CT
E3        43383     15 -->  HYPERTENSION/CT
E4            0      6      HYPERTENSION (L) BORDERLINE/CT
E5            0      6      HYPERTENSION (L) CHRONIC/CT
E6            0      6      HYPERTENSION (L) DAHL SALT-SENSITIVE/CT
E7            0      8      HYPERTENSION (L) ESSENTIAL/CT
E8            0      7      HYPERTENSION (L) GENETIC/CT
E9            0      6      HYPERTENSION (L) GOLDBLATT/CT
E10           0      2      HYPERTENSION (L) HYPOXIC PULMONARY/CT
E11           0      8      HYPERTENSION (L) INTRACRANIAL/CT
E12           0      8      HYPERTENSION (L) MALIGNANT/CT

=> e
E13           0      6      HYPERTENSION (L) MINERALOCORTICOID/CT
E14           0     13      HYPERTENSION (L) MINERALOCORTICOID SALT-SENSITIVE/CT
E15           0      7      HYPERTENSION (L) ONE-KIDNEY ONE-CLIP/CT
E16           0      7      HYPERTENSION (L) PORTAL/CT
E17           0      7      HYPERTENSION (L) PULMONARY/CT
E18           0      7      HYPERTENSION (L) PULMONARY, HYPOXIC/CT
E19           0      7      HYPERTENSION (L) RENAL/CT
E20           0      6      HYPERTENSION (L) RENOVASCULAR/CT
E21           0      6      HYPERTENSION (L) RENOVASCULAR, CHRONIC/CT
E22           0      6      HYPERTENSION (L) SALT-RESISTANT/CT
E23           0      8      HYPERTENSION (L) SALT-SENSITIVE/CT
E24           0      6      HYPERTENSION (L) SPONTANEOUS/CT

=> s e3
L28       43383 HYPERTENSION/CT

=> d his

     (FILE 'HOME' ENTERED AT 11:49:08 ON 02 MAR 2005)

     FILE 'CAPLUS' ENTERED AT 11:49:13 ON 02 MAR 2005
                E FOX DAVID/AU
L1            69 S E2-E3, E20-E22
                E HUGHES BERNADETTE/AU
L2            22 S E3-E4
                E HUGHES B/AU
L3            40 S E3
                E FOX D/AU
                E FOX D?/AU
                E FOX D/AU
L4            75 S E3
L5           144 S L1 OR L4
L6            62 S L2 OR L3
L7           204 S L5 OR L6
L8            10 S L7 AND HYPERTENSI?
L9             0 S L7 AND (CYCLIC GUANOSINE MONOPHOSPHATE (W) (PHOSPHODIESTERASE
L10            6 S L7 AND ("CGMP" OR "PDE5" OR "ANGIOTENSIN II RECEPTOR ANTAGONI

     FILE 'REGISTRY' ENTERED AT 11:57:43 ON 02 MAR 2005
                E SILDENAFIL/CN
L11            2 S E3-E4
                E TADALAFIL/CN
L12            1 S E3
                E VARDENAFIL/CN
L13            3 S E3-E5
L14            1 S CANDESARTAN/CN
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                E CANDESARTAN/CN
L15           2 S E3-E5
                E EPROSARTAN/CN
L16           2 S E3-E5
                E IRBESARTAN/CN
L17           4 S E3-E6
                E LOSARTAN/CN
L18           4 S E3-E7
                E OLMESARTAN/CN
L19           2 S E3-E5
                E SARALASIN/CN
L20           2 S E3-E4
                E TELMISARTAN/CN
L21           5 S E3-E7
                E VALSARTAN/CN
L22           2 S E3-E4
L23           6 S L11 OR L12 OR L13
L24          23 S L15 OR L16 OR L17 OR L18 OR L19 OR L20 OR L21 OR L22

     FILE 'CAPLUS' ENTERED AT 12:02:01 ON 02 MAR 2005
L25        1081 S L23
L26        4320 S L24
                E HYPERTENSION/BI
L27       78751 S E3, E16
                E HYPERTENSION/CT
L28       43383 S E3

=> s l27 or l28
L29       78751 L27 OR L28

=> s l29 or (high blood pressure) or (elevated blood pressure) or (increase? blood
pressure)
        3518588 HIGH
            539 HIGHS
        3518892 HIGH
                  (HIGH OR HIGHS)
        1174762 BLOOD
           1191 BLOODS
        1174891 BLOOD
                  (BLOOD OR BLOODS)
        1105830 PRESSURE
         165382 PRESSURES
        1168569 PRESSURE
                  (PRESSURE OR PRESSURES)
           1990 HIGH BLOOD PRESSURE
                  (HIGH(W)BLOOD(W)PRESSURE)
         240789 ELEVATED
        1174762 BLOOD
           1191 BLOODS
        1174891 BLOOD
                  (BLOOD OR BLOODS)
        1105830 PRESSURE
         165382 PRESSURES
        1168569 PRESSURE
                  (PRESSURE OR PRESSURES)
           1047 ELEVATED BLOOD PRESSURE
                  (ELEVATED(W)BLOOD(W)PRESSURE)
        3402811 INCREASE?
        1174762 BLOOD
           1191 BLOODS
        1174891 BLOOD
                  (BLOOD OR BLOODS)
        1105830 PRESSURE
         165382 PRESSURES
```

```
       1168569 PRESSURE
                 (PRESSURE OR PRESSURES)
          2223 INCREASE? BLOOD PRESSURE
                 (INCREASE?(W)BLOOD(W)PRESSURE)
L30      80818 L29 OR (HIGH BLOOD PRESSURE) OR (ELEVATED BLOOD PRESSURE) OR
               (INCREASE? BLOOD PRESSURE)

=> d his

     (FILE 'HOME' ENTERED AT 11:49:08 ON 02 MAR 2005)

     FILE 'CAPLUS' ENTERED AT 11:49:13 ON 02 MAR 2005
                 E FOX DAVID/AU
L1             69 S E2-E3, E20-E22
                 E HUGHES BERNADETTE/AU
L2             22 S E3-E4
                 E HUGHES B/AU
L3             40 S E3
                 E FOX D/AU
                 E FOX D?/AU
                 E FOX D/AU
L4             75 S E3
L5            144 S L1 OR L4
L6             62 S L2 OR L3
L7            204 S L5 OR L6
L8             10 S L7 AND HYPERTENSI?
L9              0 S L7 AND (CYCLIC GUANOSINE MONOPHOSPHATE (W) (PHOSPHODIESTERASE
L10             6 S L7 AND ("CGMP" OR "PDE5" OR "ANGIOTENSIN II RECEPTOR ANTAGONI

     FILE 'REGISTRY' ENTERED AT 11:57:43 ON 02 MAR 2005
                 E SILDENAFIL/CN
L11             2 S E3-E4
                 E TADALAFIL/CN
L12             1 S E3
                 E VARDENAFIL/CN
L13             3 S E3-E5
L14             1 S CANDESARTAN/CN
                 E CANDESARTAN/CN
L15             2 S E3-E5
                 E EPROSARTAN/CN
L16             2 S E3-E5
                 E IRBESARTAN/CN
L17             4 S E3-E6
                 E LOSARTAN/CN
L18             4 S E3-E7
                 E OLMESARTAN/CN
L19             2 S E3-E5
                 E SARALASIN/CN
L20             2 S E3-E4
                 E TELMISARTAN/CN
L21             5 S E3-E7
                 E VALSARTAN/CN
L22             2 S E3-E4
L23             6 S L11 OR L12 OR L13
L24            23 S L15 OR L16 OR L17 OR L18 OR L19 OR L20 OR L21 OR L22

     FILE 'CAPLUS' ENTERED AT 12:02:01 ON 02 MAR 2005
L25          1081 S L23
L26          4320 S L24
                 E HYPERTENSION/BI
L27         78751 S E3, E16
                 E HYPERTENSION/CT
L28         43383 S E3
L29         78751 S L27 OR L28
```

L30 80818 S L29 OR (HIGH BLOOD PRESSURE) OR (ELEVATED BLOOD PRESSURE) OR

=> s l25 and l26
L31 36 L25 AND L26

=> s l31 (L) l30
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L31 (L) L30'
L32 9 L31 (L) L30

=> s l30 and l31
L33 9 L30 AND L31

=> d l33 1-9 ibib ed abs

L33 ANSWER 1 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:77981 CAPLUS
DOCUMENT NUMBER: 142:162662
TITLE: Nanoparticulate glipizide compositions
INVENTOR(S): Bosch, H. William; Ryde, Niels P.
PATENT ASSIGNEE(S): Elan Pharma International Limited, USA
SOURCE: U.S. Pat. Appl. Publ., 24 pp., Cont.-in-part of U.S. Ser. No. 276,400.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 16
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005019412	A1	20050127	US 2003-701064	20031105
US 2002012675	A1	20020131	US 1999-337675	19990622
WO 2001087264	A2	20011122	WO 2001-US15983	20010518
WO 2001087264	A3	20020620		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 2004013613	A1	20040122	US 2003-276400	20030115
PRIORITY APPLN. INFO.:			US 1998-164351	B2 19981001
			US 1999-337675	A2 19990622
			WO 2001-US15983	W 20010518
			US 2003-276400	A2 20030115
			US 2000-572961	A 20000518

ED Entered STN: 28 Jan 2005
AB The present invention is directed to nanoparticulate compns. comprising glipizide. The glipizide particles of the composition preferably have an effective average particle size of <2 μ. Thus, a formulation contained spray-dried glipizide 5.33, mannitol 13.47, xylitol 40.53, citric acid 19.60, sodium bicarbonate 19.33, Asparatme 0.28, PEG-4000 0.93, and sodium stearyl fumarate 0.53%.

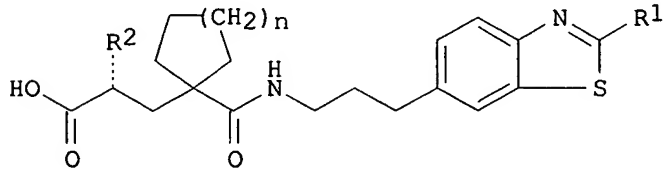
L33 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:759835 CAPLUS
DOCUMENT NUMBER: 141:277616
TITLE: Preparation of 3-(1-[3-(1,3-benzothiazol-6-yl)propylcarbamoyl]cycloalkyl)propanoic acid derivatives as nep inhibitors

INVENTOR(S): Hepworth, David
PATENT ASSIGNEE(S): Pfizer Inc., UK
SOURCE: U.S. Pat. Appl. Publ., 27 pp., which
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

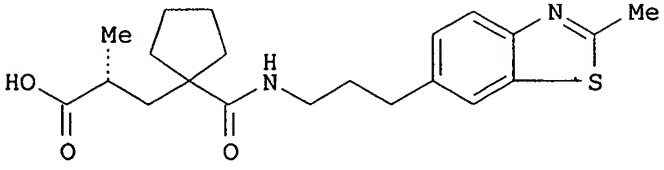
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004180941	A1	20040916	US 2004-800065	20040312
WO 2004080985	A1	20040923	WO 2004-IB822	20040309
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
NL 1025709	A1	20040916	NL 2004-1025709	20040312

PRIORITY APPLN. INFO.:	GB 2003-5916	A	20030314
	US 2003-464608P	P	20030422
	GB 2003-29143	A	20031216
	US 2004-538079P	P	20040120

OTHER SOURCE(S): MARPAT 141:277616
ED Entered STN: 17 Sep 2004
GI



I



II

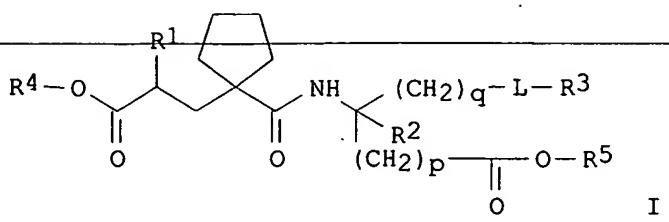
AB The invention relates to the use of title compds. I [R1 = H or Me; R2 = Me or Et; n = 1 or 2] as inhibitors of neutral endopeptidase enzyme (NEP), processes for the preparation thereof, intermediates used in the preparation thereof and compns. containing said inhibitors. Thus, e.g., II was prepared by amidation of 1-[(2R)-3-tert-butoxy-2-methyl-3-oxopropyl]cyclopentane carboxylic acid with 3-(2-methyl-1,3-benzothiazol-6-yl)propylamine dihydrochloride (preparation given) with subsequent hydrolysis to provide the free acid. I have been demonstrated to possess IC50 values of <20 nanomolar in tests for NEP inhibition and demonstrate a selectivity over

soluble secreted endopeptidase (SEP) of at least 1000 fold. These inhibitors have utility in a variety of therapeutic areas including the treatment of male and female sexual dysfunction, particularly female sexual dysfunction (FSD), especially wherein the FSD is female sexual arousal disorder (FSAD).

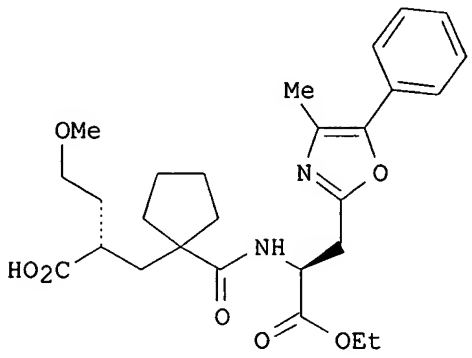
L33 ANSWER 3 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:546487 CAPLUS
DOCUMENT NUMBER: 141:106453
TITLE: Preparation of cyclopentyl glutaramide derivs. as neutral endopeptidase inhibitors
INVENTOR(S): Dack, Kevin Neil; Owen, Dafydd Rhys; Watson, Christine Anne Louise
PATENT ASSIGNEE(S): Pfizer Limited, UK; Pfizer Inc.
SOURCE: PCT Int. Appl., 109 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2004056787	A1	20040708	WO 2003-IB5981		20031212
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
US 2004138274	A1	20040715	US 2003-739426		20031218
NL 1025116	A1	20040624	NL 2003-1025116		20031223
NL 1025116	C2	20041018			
PRIORITY APPLN. INFO.:			GB 2002-30025	A	20021223
			US 2003-448224P	P	20030218

OTHER SOURCE(S): MARPAT 141:106453
ED Entered STN: 08 Jul 2004
GI



I



II

AB The title compds. I [R1 = C1-C6alkyl, C1-C6alkoxyC1-C3alkyl, or C1-C6alkoxyC1-C6alkoxyC1-C3alkyl; R2 = H or C1-C6alkyl; L = an aromatic heterocyclic ring, optionally substituted with C1-C6alkyl or halo; R3 = C1-C6alkyl optionally substituted by halo, alkoxy, haloalkoxy, alkylthio, haloalkylthio or nitrile group, or R3 is Ph or aromatic heterocyclyl each of which may be independently substituted by one or more alkyl, halo, haloalkyl, alkoxy, haloalkoxy, alkylthio, haloalkylthio or nitrile group; R4, R5 = either both hydrogen, or one of R4 and R5 is hydrogen and the other is a biolabile ester; p = 0-2; and q = 1 or 2] were prepared as neutral endopeptidase inhibitors for the treatment of cardiovascular disorders or related diseases. For example, reaction of (2S)-2-Amino-3-[5-(4-chlorophenyl)-oxazol-2-yl]-propionic acid Et ester hydrochloride (preparation given) and 1-[(2S)-2-(tert-butoxycarbonyl)-4-methoxybutyl]cyclopentanecarboxylic acid yielded (2S)-2-{1-[(1S)-1-Ethoxycarbonyl-2-(4-methyl-5-phenyl-oxazol-2-yl)-ethylcarbamoyl]-cyclopentylmethyl}-4-methoxy-butyric acid tert Bu ester, which when treated with trifluoroacetic acid furnished compound II. The prepared compds. are potent inhibitors of neutral endopeptidase.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L33 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:269863 CAPLUS

DOCUMENT NUMBER: 140:281417

TITLE: Combination therapy using antihypertensive agents and endothelin antagonists for vascular conditions associated with a male or female sexual dysfunction

INVENTOR(S): Adams, Michael A.; Hale, Taben M.; Heaton, Jeremy P. W.

PATENT ASSIGNEE(S): Queen's University At Kingston, Can.; Callegy Pharmaceuticals, Inc.

SOURCE: U.S. Pat. Appl. Publ., 29 pp., Cont.-in-part of U.S. Pat. Appl. 2003 8,020.
CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004063719	A1	20040401	US 2003-429197	20030502
US 6284763	B1	20010904	US 1999-382749	19990825
US 2002035067	A1	20020321	US 2001-902787	20010712
US 6458797	B2	20021001		
US 2003008020	A1	20030109	US 2002-192281	20020709
US 6787553	B2	20040907		
US 2004234619	A1	20041125	US 2004-869755	20040615
PRIORITY APPLN. INFO.:			US 1998-98178P	P 19980826
			US 1999-382749	A1 19990825
			US 2001-902787	A1 20010712
			US 2002-377917P	P 20020502
			US 2002-192281	A2 20020709

ED Entered STN: 02 Apr 2004

AB The present invention provides a method for a more efficacious treatment of a vascular condition through the administration of a therapeutically effective amount of a combination of an anti-pressor agent, an endothelin antagonist, and a sex hormone for repetitive cycles of on/off-treatment. In one embodiment, the invention provides a method for the prevention of tolerance induced by an anti-pressor agent via the inclusion of an endothelin antagonist in a combination therapy approach to remodel vascular structure and treat vascular conditions associated with a male or female sexual dysfunction, atherosclerosis, renal failure, **hypertension**, congestive heart failure, diabetic nephropathy, and diabetic neuropathy. The anti-pressor agent comprises one or more compds. such as prostaglandin-E 1 , an ACE inhibitor, an angiotensin-II receptor antagonist, an α1-adrenergic receptor antagonist, a β-adrenergic receptor antagonist, a calcium channel blocker, an activator of guanylyl cyclase or adenyl cyclase, a phosphodiesterase inhibitor, and hydralazine. The endothelin antagonist comprises one or more compds. such as a peptidal endothelin antagonist, a non-peptidal endothelin antagonist, and an inhibitor of endothelin converting enzyme. Such a combination therapy approach enhances the efficacy of the anti-pressor agent and enables an increase in the frequency and duration of anti-pressor administrations for the long term treatment of vascular conditions.

L33 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:60341 CAPLUS
DOCUMENT NUMBER: 140:117406
TITLE: Liquid dosage compositions of stable nanoparticulate drugs
INVENTOR(S): Bosch, William H.; Hilborn, Matthew R.; Hovey, Douglas C.; Kline, Laura J.; Lee, Robert W.; Pruitt, John D.; Ryde, Niels P.; Ryde, Tuula A.; Xu, Shuqian
PATENT ASSIGNEE(S): Elan Pharma International, Ltd, Ire.
SOURCE: PCT Int. Appl., 68 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 16
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004006959	A1	20040122	WO 2003-US22187	20030716
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN,				

TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.: US 2002-396530P P 20020716
ED Entered STN: 26 Jan 2004
AB The present invention relates to liquid dosage compns. of stable nanoparticulate drugs. The liquid dosage compns. of the invention include osmotically active crystal growth inhibitors that stabilize the nanoparticulate active agents against crystal and particle size growth of the drug. Thus, an aqueous nanoparticulate colloidal dispersion (NCD) comprising drug 32.5 Copovidone 6.5, and dioctyl sodium sulfosuccinate 0.464% by weight was prepared by milling for 3.8 h under high energy milling conditions. The final mean particle size (by weight) of the drug particles was 161 nm. The concentrated NCD was then diluted with preserved water and glycerol (the osmotically active crystal growth inhibitor) to 0.5-3.0% drug.
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L33 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:20474 CAPLUS
DOCUMENT NUMBER: 140:71026
TITLE: Novel combination for treating **hypertension**
INVENTOR(S): Fox, David Nathan Abraham; Hughes, Bernadette
PATENT ASSIGNEE(S): Pfizer, Limited, UK; Pfizer, Inc.
SOURCE: PCT Int. Appl., 25 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004002461	A2	20040108	WO 2003-IB2657	20030616
WO 2004002461	A3	20040513		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004132731	A1	20040708	US 2003-603369	20030625
PRIORITY APPLN. INFO.:			GB 2002-14784	A 20020626
			US 2002-396780P	P 20020717

ED Entered STN: 11 Jan 2004
AB Combinations comprising a) an inhibitor of cyclic guanosine monophosphate (cGMP) specific phosphodiesterase type 5 (PDE5) and b) an angiotensin II receptor antagonist are useful for treating **hypertension**. In the example provided the combined effect in **hypertensive** rats of candesartan and a PDE5 inhibitor was significantly larger than the sum of the 2 individual effects.

L33 ANSWER 7 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:396889 CAPLUS
DOCUMENT NUMBER: 138:401744
TITLE: Preparation of polycyclic guanine derivative phosphodiesterase V inhibitors

INVENTOR(S): Asberom, Theodros; Clader, John W.; Hu, Yueqing; Pissarnitski, Dmitri A.; Stamford, Andrew W.; Xu, Ruo

PATENT ASSIGNEE(S): Schering Corporation, USA

SOURCE: PCT Int. Appl., 95 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003042216	A1	20030522	WO 2002-US35721	20021107
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MA, MD, MG, MK, MN, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SC, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UZ, VC, VN, YU, ZA, ZM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003176413	A1	20030918	US 2002-290011	20021107
EP 1442042	A1	20040804	EP 2002-786685	20021107
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				

PRIORITY APPLN. INFO.: US 2001-344498P P 20011109
WO 2002-US35721 W 20021107

OTHER SOURCE(S): MARPAT 138:401744

ED Entered STN: 23 May 2003

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [q = 0-2; R1, R3-6 = H, alkyl, aryl, heteroaryl, cycloalkyl, heterocycloalkyl; R2 = H, halo, alkyl, alkoxy, etc.; Y = alkyl, aryl] are prepared For instance, 4-amino-1-benzyl-5-(ethoxycarbonyl)imidazole (preparation given) is treated with ethylisocyanate (o-xylene, reflux, 16 h), the resulting product cyclized (MeOH, NaOMe, reflux, 4 h), subsequently treated with POCl3 and the product used to alkylate (R)-2-amino-3-phenylpropanol (NMP, 130°, 12 h) which provides II. II is treated with MsCl (Et3N), debenzylated (MeOH, NH4O2CH, Pd(OH)2/C, reflux, 3 h), brominated (HOAc, NaOAc, Br2), alkylated with 3-chloro-4-methoxybenzyl bromide (DMF, K2CO3) and treated with NaOEt (DMF/EtOH) to afford III. III has IC50 < 4.1 nM for PDE V and IC50 > 300 nM for PDE VI. I are useful for treating sexual dysfunction.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L33 ANSWER 8 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:338762 CAPLUS

DOCUMENT NUMBER: 134:362292

TITLE: Methods of determining individual hypersensitivity to a pharmaceutical agent from gene expression profile

INVENTOR(S): Farr, Spencer

PATENT ASSIGNEE(S): Phase-1 Molecular Toxicology, USA

SOURCE: PCT Int. Appl., 222 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001032928	A2	20010510	WO 2000-US30474	20001103
WO 2001032928	A3	20020725		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-165398P P 19991105
US 2000-196571P P 20000411

ED Entered STN: 11 May 2001

AB The invention discloses methods, gene databases, gene arrays, protein arrays, and devices that may be used to determine the hypersensitivity of individuals to a given agent, such as drug or other chemical, in order to prevent toxic side effects. In one embodiment, methods of identifying hypersensitivity in a subject by obtaining a gene expression profile of multiple genes associated with hypersensitivity of the subject suspected to be hypersensitive, and identifying in the gene expression profile of the subject a pattern of gene expression of the genes associated with hypersensitivity are disclosed. The gene expression profile of the subject may be compared with the gene expression profile of a normal individual and a hypersensitive individual. The gene expression profile of the subject that is obtained may comprise a profile of levels of mRNA or cDNA. The gene expression profile may be obtained by using an array of nucleic acid probes for the plurality of genes associated with hypersensitivity. The expression of the genes predetd. to be associated with hypersensitivity is directly related to prevention or repair of toxic damage at the tissue, organ or system level. Gene databases arrays and apparatus useful for identifying hypersensitivity in a subject are also disclosed.

L33 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:161149 CAPLUS
DOCUMENT NUMBER: 132:203141
TITLE: Anti-pressor agents and methods for remodeling neuronal and cardiovascular pathways for the long term management of sexual dysfunction
INVENTOR(S): Adams, Michael A.; Heaton, Jeremy P. W.
PATENT ASSIGNEE(S): Queen's University At Kingston, Can.
SOURCE: PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000012110	A2	20000309	WO 1999-CA787	19990825
WO 2000012110	A3	20000803		

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK,

ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

CA 2340206		AA	20000309	CA 1999-2340206	19990825
AU 9954034		A1	20000321	AU 1999-54034	19990825
EP 1235563		A2	20020904	EP 1999-939874	19990825
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL					
PRIORITY APPLN. INFO.:				US 1998-98178P	P 19980826
				WO 1999-CA787	W 19990825

ED Entered STN: 10 Mar 2000

AB The invention provides a method of administration of an agent which acts to remodel neuronal or vascular pathways for the long term management of sexual dysfunction in both males and females. In a preferred embodiment, the invention provides a method of ameliorating or reversing pathogenic vascular degradative modeling in the ilio-hypogastric-pudendal arterial bed and genitalia comprising administering to a human patient in need of such treatment a therapeutically effective amount of an anti-pressor agent. The anti-pressor agent comprises one or more compds. selected from the therapeutic classes of direct vasodilators such as hydralazine and NO donors, ACE inhibitors, angiotensin-II receptor antagonists, α1-adrenergic receptor antagonists, β-adrenergic receptor antagonists, calcium channel blockers, and phosphodiesterase inhibitors. The anti-pressor agent may be co-administered with a diuretic compound, and is administered either chronically at low dose, or for short periods of time at doses higher than are typically used for the treatment of **hypertension**. In certain embodiments of the method of the invention, the anti-pressor agent is co-administered with a diuretic agent and/or prostaglandin-E1.

=> d his

(FILE 'HOME' ENTERED AT 11:49:08 ON 02 MAR 2005)

FILE 'CAPLUS' ENTERED AT 11:49:13 ON 02 MAR 2005

	E	FOX DAVID/AU
L1	69	S E2-E3, E20-E22
	E	HUGHES BERNADETTE/AU
L2	22	S E3-E4
	E	HUGHES B/AU
L3	40	S E3
	E	FOX D/AU
	E	FOX D?/AU
	E	FOX D/AU
L4	75	S E3
L5	144	S L1 OR L4
L6	62	S L2 OR L3
L7	204	S L5 OR L6
L8	10	S L7 AND HYPERTENSI?
L9	0	S L7 AND (CYCLIC GUANOSINE MONOPHOSPHATE (W) (PHOSPHODIESTERASE
L10	6	S L7 AND ("CGMP" OR "PDE5" OR "ANGIOTENSIN II RECEPTOR ANTAGONI

FILE 'REGISTRY' ENTERED AT 11:57:43 ON 02 MAR 2005

	E	SILDENAFIL/CN
L11	2	S E3-E4
	E	TADALAFIL/CN
L12	1	S E3
	E	VARDENAFIL/CN
L13	3	S E3-E5
L14	1	S CANDESARTAN/CN
	E	CANDESARTAN/CN
L15	2	S E3-E5
	E	EPROSARTAN/CN
L16	2	S E3-E5

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                E IRBESARTAN/CN
L17           4 S E3-E6
                E LOSARTAN/CN
L18           4 S E3-E7
                E OLMESARTAN/CN
L19           2 S E3-E5
                E SARALASIN/CN
L20           2 S E3-E4
                E TELMISARTAN/CN
L21           5 S E3-E7
                E VALSARTAN/CN
L22           2 S E3-E4
L23           6 S L11 OR L12 OR L13
L24          23 S L15 OR L16 OR L17 OR L18 OR L19 OR L20 OR L21 OR L22

     FILE 'CAPLUS' ENTERED AT 12:02:01 ON 02 MAR 2005
L25        1081 S L23
L26        4320 S L24
                E HYPERTENSION/BI
L27       78751 S E3, E16
                E HYPERTENSION/CT
L28       43383 S E3
L29       78751 S L27 OR L28
L30       80818 S L29 OR (HIGH BLOOD PRESSURE) OR (ELEVATED BLOOD PRESSURE) OR
L31          36 S L25 AND L26
L32           9 S L31 (L) L30
L33           9 S L30 AND L31

=> s l25 (L) l30
L34          34 L25 (L) L30

=> s l26 (L) l30
L35        1025 L26 (L) L30

=> s l34 and l35
L36           0 L34 AND L35

=> s l31 and hypertens?
         79500 HYPERTENS?
L37           9 L31 AND HYPERTENS?

=> s l37 not l33
L38           0 L37 NOT L33

=> s "CGMP" or "PDE5" or (cyclic guanosine monophosphate (w) phosphodiesterase)
         20057 "CGMP"
           187 "CGMPS"
         20081 "CGMP"
                 ("CGMP" OR "CGMPS")
           533 "PDE5"
        286246 CYCLIC
           330 CYCLICS
        286374 CYCLIC
                 (CYCLIC OR CYCLICS)
         21456 GUANOSINE
           313 GUANOSINES
         21565 GUANOSINE
                 (GUANOSINE OR GUANOSINES)
         29181 MONOPHOSPHATE
          3848 MONOPHOSPHATES
         31896 MONOPHOSPHATE
                 (MONOPHOSPHATE OR MONOPHOSPHATES)
           835 CYCLIC GUANOSINE MONOPHOSPHATE
                 (CYCLIC(W)GUANOSINE(W)MONOPHOSPHATE)
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         24057 PHOSPHODIESTERASE
          2560 PHOSPHODIESTERASES
         24563 PHOSPHODIESTERASE
                 (PHOSPHODIESTERASE OR PHOSPHODIESTERASES)
            33 CYCLIC GUANOSINE MONOPHOSPHATE (W) PHOSPHODIESTERASE
L39      20335 "CGMP" OR "PDE5" OR (CYCLIC GUANOSINE MONOPHOSPHATE (W) PHOSPHOD
               IESTERASE)

=> s (angiotensin (L) receptor antagonist) or (angiotensin receptor antagonist) or
"angiotensin II receptor antagonist"
         54762 ANGIOTENSIN
          1691 ANGIOTENSINS
         54850 ANGIOTENSIN
                 (ANGIOTENSIN OR ANGIOTENSINS)
        591069 RECEPTOR
        542204 RECEPTORS
        703691 RECEPTOR
                 (RECEPTOR OR RECEPTORS)
        149224 ANTAGONIST
        108335 ANTAGONISTS
        200876 ANTAGONIST
                 (ANTAGONIST OR ANTAGONISTS)
         66210 RECEPTOR ANTAGONIST
                 (RECEPTOR(W)ANTAGONIST)
          6539 ANGIOTENSIN (L) RECEPTOR ANTAGONIST
         54762 ANGIOTENSIN
          1691 ANGIOTENSINS
         54850 ANGIOTENSIN
                 (ANGIOTENSIN OR ANGIOTENSINS)
        591069 RECEPTOR
        542204 RECEPTORS
        703691 RECEPTOR
                 (RECEPTOR OR RECEPTORS)
        149224 ANTAGONIST
        108335 ANTAGONISTS
        200876 ANTAGONIST
                 (ANTAGONIST OR ANTAGONISTS)
          2785 ANGIOTENSIN RECEPTOR ANTAGONIST
                 (ANGIOTENSIN(W)RECEPTOR(W)ANTAGONIST)
         54762 "ANGIOTENSIN"
          1691 "ANGIOTENSINS"
         54850 "ANGIOTENSIN"
                 ("ANGIOTENSIN" OR "ANGIOTENSINS")
       2015064 "II"
           825 "IIS"
       2015534 "II"
                 ("II" OR "IIS")
        591069 "RECEPTOR"
        542204 "RECEPTORS"
        703691 "RECEPTOR"
                 ("RECEPTOR" OR "RECEPTORS")
        149224 "ANTAGONIST"
        108335 "ANTAGONISTS"
        200876 "ANTAGONIST"
                 ("ANTAGONIST" OR "ANTAGONISTS")
          1675 "ANGIOTENSIN II RECEPTOR ANTAGONIST"
                 ("ANGIOTENSIN"(W)"II"(W)"RECEPTOR"(W)"ANTAGONIST")
L40       6539 (ANGIOTENSIN (L) RECEPTOR ANTAGONIST) OR (ANGIOTENSIN RECEPTOR
               ANTAGONIST) OR "ANGIOTENSIN II RECEPTOR ANTAGONIST"

=> s l39 (L) l40
L41         80 L39 (L) L40

=> s l41 and hypertens?
```

```
         79500 HYPERTENS?
L42          17 L41 AND HYPERTENS?
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=> s l42 not l33
L43          16 L42 NOT L33

=> d l43 1-16 ibib ed abs

L43  ANSWER 1 OF 16  CAPLUS  COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:         2004:965255  CAPLUS
DOCUMENT NUMBER:          141:410950
TITLE:                    Preparation of 5,7-diaminopyrazolo[4,3-d]pyrimidines
                          as selective PDE5 inhibitors useful in the treatment
                          of hypertension
INVENTOR(S):              Bell, Andrew Simon; Brown, David Graham; Fox, David
                          Nathan Abraham; Marsh, Ian Roger; Morrell, Andrew Ian;
                          Palmer, Michael John; Winslow, Carol Ann
PATENT ASSIGNEE(S):       Pfizer Limited, UK; Pfizer Inc.
SOURCE:                   PCT Int. Appl., 279 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.          DATE
     ---------------      ----   --------    -------------------      --------
     WO 2004096810         A1    20041111    WO 2004-IB1433           20040422
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
             LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
             NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
             TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
             BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE,
             ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI,
             SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN,
             TD, TG
     NL 1026074            A1    20041101    NL 2004-1026074          20040428
     US 2005043325         A1    20050224    US 2004-834484           20040429
PRIORITY APPLN. INFO.:                       GB 2003-9780         A   20030429
                                             GB 2003-27748        A   20031128
                                             US 2003-476678P      P   20030606
                                             US 2004-538147P      P   20040120
OTHER SOURCE(S):          MARPAT 141:410950
ED   Entered STN:  12 Nov 2004
GI
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* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [wherein R1 = (un)substituted cycloalkyl, cycloalkenyl, (un)substituted pyridin-2-yl, (un)fused Ph, etc.; R2 = H, alkyl; R3, R4 = independently (un)substituted alkyl, alkenyl, cycloalkyl, etc.; or NR3R4 = piperazin-1-yl, monocyclic, saturated polycyclic; R5 = (un)substituted halo/alkyl, alkenyl, alkynyl, cycloalkyl; R6 = H, (un)substituted alkyl, haloalkyl, alkenyl, alkynyl, etc.] were prepared as selective PDE5 inhibitors. For example, II•2HCl was prepared from (4-Methylpyridin-2-yl)amine, dichloride III (general preparation given), and tert-Bu piperazine-1-carboxylate. I gave IC50 values < 10,000 nM in an in vitro assay for PDE5 inhibition. Thus, I are used for treating

hypertension.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L43 ANSWER 2 OF 16 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:884340 CAPLUS
DOCUMENT NUMBER: 141:389246
TITLE: Angiotensin-(1-7) Inhibitory Mechanism of Norepinephrine Release in **Hypertensive** Rats
AUTHOR(S): Gironacci, Mariela M.; Valera, Maria S.; Yujnovsky, Irene; Pena, Clara
CORPORATE SOURCE: Departamento de Quimica Biologica, Instituto de Quimica y Fisicoquimica Biologicas, Facultad de Farmacia y Bioquimica, Universidad de Buenos Aires, Argent.
SOURCE: Hypertension (2004), 44(5), 783-787
CODEN: HPRTDN; ISSN: 0194-911X
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 25 Oct 2004
AB Release of norepinephrine (NE) by the hypothalamic nuclei may contribute to regulation of sympathetic nervous system (SNS) activity. **Angiotensin**-(1-7) [Ang-(1-7)] has an antihypertensive effect and may decrease SNS activity. We tested the hypothesis that Ang-(1-7) inhibits the release of NE in hypothalami, via the Ang-(1-7) and **angiotensin** II type 2 (AT2) receptors, acting through a bradykinin (BK)/NO-dependent mechanism. Hypothalami from normotensive controls and spontaneously **hypertensive** rats (SHR) were isolated and endogenous NE stores labeled by incubating the tissues with [3H]NE. [3H]NE release from the hypothalami was stimulated by KCl in the presence or absence of Ang-(1-7) alone or combined with various antagonists and inhibitors. Ang-(1-7) significantly attenuated K+-induced NE release by hypothalami from normotensive rats but was more potent in SHR. The Ang-(1-7) **receptor antagonist** [D-Ala7]Ang-(1-7), the AT2 **receptor antagonist** PD 123319, and the BK B2 **receptor antagonist** icatibant all blocked the inhibitory effect of Ang-(1-7) on K+-stimulated NE release in SHR. The inhibitory effect of Ang-(1-7) disappeared in the presence of the NO synthase inhibitor NG-nitro-L-arginine Me ester and was restored by the precursor of NO, L-arginine. The diminished NE release caused by Ang-(1-7) was blocked by a soluble guanylyl cyclase inhibitor as well as by a **cGMP**-dependent protein kinase (PKG). We concluded that Ang-(1-7) decreases NE release from the hypothalamus via the Ang-(1-7) or AT2 receptors, acting through a BK/NO-mediated mechanism that stimulates **cGMP**/PKG signaling. In this way, Ang-(1-7) may decrease SNS activity and exert an antihypertensive effect.
REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L43 ANSWER 3 OF 16 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:544960 CAPLUS
DOCUMENT NUMBER: 141:188914
TITLE: RhoA activation in vascular smooth muscle cells from stroke-prone spontaneously **hypertensive** rats
AUTHOR(S): Moriki, Nobuyuki; Ito, Masaaki; Seko, Tetsuya; Kureishi, Yasuko; Okamoto, Ryuji; Nakakuki, Tetsuya; Kongo, Mariko; Isaka, Naoki; Kaibuchi, Kozo; Nakano, Takeshi
CORPORATE SOURCE: First Department of Internal Medicine, Mie University School of Medicine, Tsu, Japan
SOURCE: Hypertension Research (2004), 27(4), 263-270
CODEN: HRESE4; ISSN: 0916-9636
PUBLISHER: Japanese Society of Hypertension

DOCUMENT TYPE: Journal
LANGUAGE: English

ED Entered STN: 08 Jul 2004

AB RhoA is commonly activated in the aorta in various **hypertensive** models, indicating that RhoA seems to be a mol. switch in **hypertension**. The mol. mechanisms for RhoA activation in stroke-prone spontaneously **hypertensive** rats (SHRSP) were here investigated using cultured aortic smooth muscle cells (VSMC). The level of the active form of RhoA was higher in VSMC from SHRSP than in those from Wistar-Kyoto rats (WKY). The phosphorylation level of myosin phosphatase target subunit 1 (MYPT1) at the inhibitory site was also significantly higher in SHRSP, and the phosphorylation levels in both VSMCs were strongly inhibited to a similar extent by treatment with Y-27632, a Rho-kinase inhibitor. The expression levels of RhoA/Rho-kinase related mols., namely RhoA, Rho-kinase, MYPT1, CPI-17 (inhibitory phosphoprotein for myosin phosphatase) and myosin light chain kinase, were not different between SHRSP and WKY. Valsartan, an **angiotensin** II (Ang II)-type 1 **receptor antagonist**, selectively and significantly reduced the RhoA activation in VSMC from SHRSP. The expression levels of the Rho GDP-dissociation inhibitor (RhoGDI) and leukemia-associated Rho-specific guanine nucleotide exchange factor (RhoGEF) did not differ between SHRSP and WKY. In cyclic nucleotide signaling, cyclic GMP (**cGMP**)-dependent protein kinase Iα (cGKIα) was significantly downregulated in SHRSP cells, although there were no changes in the expression levels of guanylate cyclase β and cAMP-dependent protein kinase or the intracellular contents of **cGMP** and cAMP between the two rat models. These results suggest that the possible mechanisms underlying RhoA activation in VSMC from SHRSP are autocrine/paracrine regulation by Ang II and/or cGKIα downregulation.

L43 ANSWER 4 OF 16 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:296093 CAPLUS
DOCUMENT NUMBER: 141:307251
TITLE: Effect of angiotensin II type 1 (at1) receptor antagonist on the endothelial dysfunction in spontaneously **hypertensive** rats in correlation with the nitric oxide system
AUTHOR(S): Slaninka-Miceska, M.; Bogdanska, J.; Korneti, P.; Kostova, E.; Jovanoska, E.; Petrov, S.
CORPORATE SOURCE: Medical Faculty, Department of Preclinical and Clinical Pharmacology and Toxicology, Skopje, Macedonia
SOURCE: Bratislavske Lekarske Listy (2003), 104(11), 342-346
CODEN: BLLIAX; ISSN: 0006-9248
PUBLISHER: Slovak Academic Press Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

ED Entered STN: 12 Apr 2004

AB Background: **Hypertension** is associated with impaired endothelial function, which can be explained by a decrease in nitric oxide (NO) generation or by an enhanced inactivation of NO after its release from endothelial cells. Objectives: The aim of this study was to investigate the effect of long-term treatment with losartan, an **angiotensin** II (AT1) **receptor antagonist**, on endothelial dysfunction in an animal model of **hypertension** in relation to the nitric oxide system. Methods: Losartan was administered to 48 sixteen-week-old spontaneously **hypertensive** rats, in a dose of 10 mg/kg bw/daily in drinking water, for 12 wk. Systolic blood pressure (SBP) was measured at the beginning, after 4, 8 and 12 wk of treatment, by the tail-cuff plethysmog. method. At each mentioned time point, a group of 12 animals was sacrificed and blood was withdrawn from the abdominal aorta. Plasma samples were used for determination of total nitrate/nitirite levels, cyclic guanosine monophosphate (**cGMP**) and endothelin

(ET) 1 levels. Statistical evaluation of the results was performed by the use of a computer statistical program Statistica for Windows 5.0. Results: Losartan produced a significant decrease of SBP at all time points. On the other hand, long-term treatment with this AT1 **receptor antagonist** produced a significant increase of nitrate/nitrite and **cGMP** plasma levels. When we compared the values of SBP with plasma nitrate/nitrite as well as with **cGMP** values, a statistically significant correlation was established. A statistically significant decrease in plasma endothelin 1 values was found during the whole study period. Also, a pos. correlation between SBP and plasma endothelin 1 concns. was observed Conclusions: Long-term losartan (AT1 **receptor antagonist**) treatment, apart from its blood pressure lowering effect in **hypertension**, has beneficial effects on the endothelial dysfunction which is at least partially due to the activation of the nitric oxide system.

REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L43 ANSWER 5 OF 16 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:273646 CAPLUS
DOCUMENT NUMBER: 139:177918
TITLE: The vascular response to the K+ channel inhibitor 4-aminopyridine in **hypertensive** rats
AUTHOR(S): Berg, Torill
CORPORATE SOURCE: Institute for Basic Medical Sciences, Department of Physiology, University of Oslo, Oslo, 0317, Norway
SOURCE: European Journal of Pharmacology (2003), 466(3), 301-310
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 09 Apr 2003
AB The K+ channel inhibitor 4-aminopyridine induced an immediate increase in blood pressure and tension in spontaneously **hypertensive** rats (SHR). Further anal. strongly suggested this to be due to closure of vascular smooth muscle K+ channels, as previously concluded for normotensive rats (WKY). The tension response was greater in SHR than WKY, suggesting an increased channel activity to compensate for the high total peripheral vascular resistance in SHR. The response was enhanced after nitric oxide (NO) synthase inhibitor in both strains, probably reflecting increased channel activity after elimination of the NO-**cGMP** pathway. The response in SHR but not WKY was increased after α1-adrenoceptor inhibition and adrenalectomy but not sympathetic nerve transmitter depletion. It increased also after **angiotensin** AT1 and endothelin ETA **receptor antagonists** and protein kinase C inhibitor. These results indicated an increased adrenal catecholamine, **angiotensin** AT1 and endothelin ETA activation of the phospholipase C-protein kinase C pathway in SHR, inhibiting the 4-aminopyridine-sensitive K+ channels.

REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L43 ANSWER 6 OF 16 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:526570 CAPLUS
DOCUMENT NUMBER: 138:100636
TITLE: Dual ACE and NEP inhibitor MDL-100,240 prevents and regresses severe angiotensin II-dependent **hypertension** partially through bradykinin type 2 receptor
AUTHOR(S): Rossi, Gian Paolo; Cavallin, Martina; Rizzoni, Damiano; Bova, Sergio; Mazzocchi, Giuseppina; Agabiti-Rosei, Enrico; Nussdorfer, Gastone G.; Pessina, Achille C.

CORPORATE SOURCE: Department of Medical and Surgical Sciences, University of Brescia, Brescia, Italy

SOURCE: Journal of Hypertension (2002), 20(7), 1451-1459
CODEN: JOHYD3; ISSN: 0263-6352
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 16 Jul 2002

AB To investigate the effects of the dual **angiotensin**-converting enzyme (ACE) + neutral endopeptidase (NEP) inhibitor, MDL-100,240 (MDL), on **hypertension** and cardiovascular damage in male heterozygous transgenic Ren2 rats. Blood-pressure-matched 5-wk-old transgenic rats were allocated to receive a placebo, MDL (40 mg/kg body weight) or ramipril (5 mg/kg body weight) for 8 wk. During the last 4 wk, the bradykinin B2 **receptor antagonist**, icatibant (0.5 mg/kg body weight), was also administered s.c. via osmotic minipumps to 50% of the transgenic rats receiving MDL or ramipril. We measured blood pressure, heart weight, structural changes in the aorta and small resistance mesenteric arteries, and the plasma concns. of adrenomedullin, aldosterone, atrial natriuretic peptide and **cGMP**. To verify if MDL could regress long-standing **hypertension** and full-blown cardiovascular damage, 3-mo-old transgenic rats received MDL s.c. (3 and 10 mg/kg body weight, osmotic minipumps) for 4 wk. Compared with placebo, MDL decreased blood pressure ($P < 0.001$) and prevented left ventricular hypertrophy ($P < 0.001$), being as effective as ramipril. Hypertrophy and dilatation of the aorta and hypertrophy of the resistance arterioles were all prevented by MDL. Plasma aldosterone was decreased by MDL ($P < 0.001$), but not by ramipril. Icatibant blunted the decrease in blood pressure ($P < 0.001$), decreased **cGMP** concns. and blunted the decrease in cross-sectional area of the resistance arteries in MDL-treated, but not in ramipril-treated, transgenic rats. In 3-mo-old transgenic rats, MDL normalized blood pressure, regressed left ventricular hypertrophy and decreased adrenomedullin concns. The dual ACE+NEP inhibitor MDL prevented and regressed severe **hypertension** and cardiovascular damage, even in this model of severe **angiotensin** II-dependent **hypertension** with pronounced cardiovascular damage. Enhancement of the effects of bradykinin has a role in such favorable outcomes.

REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L43 ANSWER 7 OF 16 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:469978 CAPLUS
DOCUMENT NUMBER: 137:367891

TITLE: Renoprotective Mechanisms of Angiotensin II Antagonism in Experimental Chronic Renal Failure

AUTHOR(S): Uhlenius, Nina; Miettinen, Aaro; Vuolteenaho, Olli; Tikkanen, Ilkka
CORPORATE SOURCE: Haartman Institute, Minerva Foundation Institute for Medical Research, University of Helsinki, Helsinki, Finland

SOURCE: Kidney & Blood Pressure Research (2002), 25(2), 71-79
CODEN: KBPRFC; ISSN: 1420-4096
PUBLISHER: S. Karger AG
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 24 Jun 2002

AB Aims: We investigated **angiotensin** II and nitric oxide-**cGMP** pathway in the development of **hypertension** and renal damage in chronic exptl. nephritis. Methods: Rats with autoimmune nephritis were treated for 12 wk with AT1 **receptor antagonist** L-158,809 and/or ACE inhibitor captopril given in drinking water. Blood pressure, urinary albumin, and urinary excretion of **cGMP** were measured. Renal d. of ACE, AT1 and AT2 receptors was determined by quant. in vitro autoradiog. Results: L-158,809, captopril, and

their combination decreased blood pressure and normalized urinary albumin excretion rate in rats with nephritis. In L-158,809-treated rats, **cGMP** excretion was increased compared to the vehicle-treated nephritic group suggesting that the dysfunctional nitric oxide system may be activated by **angiotensin** antagonism. In nephritic rats, AT1 and AT2 receptor binding densities in renal medulla were decreased, cortical AT receptor expression remained unchanged. Following L-158,809 treatment, both AT1 and AT2 receptor binding was suppressed. Conclusion: Long-term blockade of AT1 receptors in chronic nephritis has beneficial effects both on albuminuria and blood pressure being as effective as ACE inhibition or their combination. The stimulatory effect of AT1 receptor antagonism on **cGMP** production was not mediated by AT2 receptor-dependent mechanisms suggesting that AT1 receptor blockade per se favors activation of humoral pathways that stimulate **cGMP** production and potentially contribute to renal protection in chronic nephritis.

REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L43 ANSWER 8 OF 16 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:145890 CAPLUS
DOCUMENT NUMBER: 137:195283
TITLE: Renin-angiotensin blockade improves renal cGMP production via non-AT2-receptor mediated mechanisms in **hypertension**-induced by chronic NOS inhibition in rat
AUTHOR(S): Uhlenius, Nina; Vuolteenaho, Olli; Tikkanen, Ilkka
CORPORATE SOURCE: Institute for Medical Research, Minerva Foundation, Helsinki, FIN-00250, Finland
SOURCE: JRAAS (2001), 2(4), 233-239
CODEN: JRAAAG; ISSN: 1470-3203
PUBLISHER: JRAAS Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 26 Feb 2002
AB Background To investigate the changes in the **angiotensin** II (Ang II) receptors and nitric oxide (NO)-**cGMP** pathway in the rat kidney after nitric oxide synthase (NOS) blockade. Methods Captopril, an **angiotensin**-converting enzyme (ACE) inhibitor, 20 mg/100 mL; and/or L-158,809 (an Ang II AT1-**receptor antagonist**, 5 mg/100 mL) and L-NAME (NOS inhibitor, 50 mg/100 mL) were administered orally for 12 wk. Blood pressure (BP), urinary albumin, urinary **cGMP** excretion, plasma ANP, and plasma renin activity were measured. In vitro autoradiog. was used to locate the Ang II receptors in the kidney. Results Captopril and L-158,809 treatments normalized BP and prevented the appearance of albuminuria in rats receiving L-NAME. Urinary **cGMP** excretion was significantly increased in L-158,809-treated rats compared with the non-treated group, suggesting that the dysfunctional NO system may be activated by the treatment. AT1-receptor binding in the kidney was inhibited to about 40% of the control value after administration of L-158,809. The AT2-receptor binding was inhibited to less than 15% of the control value. NOS inhibition had no effect on receptor binding. Conclusion Blockade of NOS causes **hypertension** and renal damage. Treatment with an ACE inhibitor and/or Ang II **receptor antagonist** prevented these changes equally effectively. The stimulatory effect of AT1-receptor antagonism on **cGMP** production was not mediated by AT2-receptor-dependent mechanisms, since renal AT2-receptor binding d. was suppressed following treatment with L-158,809. AT1-receptor blockade per se favors activation of humoral pathways that stimulate **cGMP** production potentially contributing to renal and vascular protection in **hypertension** and chronic renal disease.

REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L43 ANSWER 9 OF 16 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:614955 CAPLUS
DOCUMENT NUMBER: 135:366494
TITLE: Angiotensin-converting enzyme inhibition potentiates angiotensin II type 1 receptor effects on renal bradykinin and cGMP
AUTHOR(S): Siragy, Helmy M.; De Gasparo, Marc; El-Kersh, Mohamed; Carey, Robert M.
CORPORATE SOURCE: Department of Medicine, University of Virginia Health Sciences Center, Charlottesville, VA, 22908, USA
SOURCE: Hypertension (2001), 38(2), 183-186
CODEN: HPRTDN; ISSN: 0194-911X
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 24 Aug 2001
AB Angiotensin (Ang) receptor blockers (ARBs) increase bradykinin (BK) by antagonizing Ang II at its type I (AT1) receptors and diverting Ang II to its counterregulatory type 2 (AT2) receptors. Because the effect of ARBs on BK is constrained by the short half-life of BK and because ACE inhibitors block the degradation of BK, this study was designed to test the hypothesis that an ACE inhibitor can potentiate ARB-induced increases in renal interstitial fluid (RIF) BK levels. The authors used a microdialysis technique to recover BK and cGMP in vivo from the RIF of sodium-depleted, conscious Sprague-Dawley rats infused for 60 min with the AT2 receptor blocker valsartan (0.17 mg/kg per min), with the active metabolite of the ACE inhibitor benazepril (benazeprilat. 0.05 mg/kg per min), or with the specific AT2 receptor blocker PD 123,319 (50 μg/kg per min) alone or combined. Each animal served as its own control. RIF BK and cGMP levels increased significantly over 1 h in response to valsartan, benazeprilat, or both but not to a vehicle control. The combined benazeprilat-valsartan effect was greater than the sum of their individual effects. suggesting potentiation rather than addition, and was abolished by PD 123,319. The authors demonstrate for the first time that an ACE inhibitor (benazepril) and an ARB (valsartan) potentiate each other, and the authors postulate that such combinations may be beneficial in clin. states marked by Ang II elevation, such as chronic heart failure, postinfarction left ventricular dysfunction, and **hypertension**.
REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L43 ANSWER 10 OF 16 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:337384 CAPLUS
TITLE: Patent focus on agents affecting cardiovascular and renal functions november 1999 - march 2000
AUTHOR(S): Lemmens-Gruber, Rosa
CORPORATE SOURCE: Institute of Pharmacology and Toxicology, University of Vienna, Vienna, A-1090, Austria
SOURCE: Expert Opinion on Therapeutic Patents (2000), 10(5), 533-548
CODEN: EOTPEG; ISSN: 1354-3776
PUBLISHER: Ashley Publications Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 21 May 2000
AB Patent applications relevant to therapy of cardiovascular diseases are reviewed for the period of Nov. 1999 to Mar. 2000. Most of the patents discussed deal with agents affecting blood clotting, membrane ionic currents, **hypertension** and hypercholesterolemia. The development and evaluation of several new therapeutic agents for treatment of blood coagulation disorders are discussed, including glycoprotein (GP) IIb/IIIa antagonists, activators of protease-activated receptors, P2T **receptor antagonists**, adenosine receptor agonists and serine protease inhibitors. Interesting new blockers of the sodium-proton

exchange, the N-type calcium channels and the ultrarapid delayed rectifier potassium current (IKur) are introduced. Antihypertensive agents are presented including **angiotensin II receptor antagonists**, vasopressin antagonists and phosphodiesterase inhibitors. Compds. effective against hypercholesterolemia, especially inhibitors of cholesterol ester transfer protein (CETP) and acyl CoA:cholesterol acyltransferase (ACAT) are also addressed. Agents acting via other mechanisms, like the nitric oxide-**cGMP** (NO-**cGMP**) pathway, that are involved in cardiovascular effects are discussed.

REFERENCE COUNT: 86 THERE ARE 86 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L43 ANSWER 11 OF 16 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:370989 CAPLUS
DOCUMENT NUMBER: 131:168631
TITLE: Protective role of the angiotensin AT2 receptor in a renal wrap **hypertension** model
AUTHOR(S): Siragy, Helmy M.; Carey, Robert M.
CORPORATE SOURCE: Department of Medicine, University of Virginia Health Sciences Center, Charlottesville, VA, USA
SOURCE: Hypertension (1999), 33(5), 1237-1242
CODEN: HPRTDN; ISSN: 0194-911X
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 15 Jun 1999
AB We evaluated the role of the renal **angiotensin** II type 2 (AT2) receptor in blood pressure regulation in rats with 2-kidney, 1 figure-8 wrap (Grollman) **hypertension**. Renal wrapping increased systolic blood pressure (SBP). Renal interstitial fluid (RIF) bradykinin (BK), nitric oxide end-products (NOX), and **cGMP** were higher in the contralateral intact kidney than in the wrapped kidney. In rats with Grollman **hypertension**, losartan normalized SBP and increased renal function, RIF BK, NOX, and **cGMP** only in contralateral kidneys. In contrast, PD 123319, a specific AT2-**receptor antagonist**, significantly increased SBP and decreased RIF BK, NOX, and **cGMP** in both kidneys. Combined administration of losartan and PD 123319 prevented the decrease in SBP and the increase in RIF BK, NOX, and **cGMP** levels observed with losartan alone. BK-receptor blockade caused a significant increase in RIF BK and a decrease in RIF NOX and **cGMP** in both kidneys similar to that observed during administration of PD 123319. In rats that underwent sham operation, RIF BK increased in response to **angiotensin** II, an effect that was blocked by PD 123319. These data demonstrate that **angiotensin** II mediates renal production of BK, which, in turn, releases nitric oxide and **cGMP** via stimulation of AT2 receptors. The increase in blood pressure and the decrease in renal BK, nitric oxide, and **cGMP** during AT2-receptor blockade suggests that the AT2 receptor mediates counterregulatory vasodilation in Grollman **hypertension** and prevents a further increase in blood pressure.
REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L43 ANSWER 12 OF 16 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:1198 CAPLUS
DOCUMENT NUMBER: 130:204863
TITLE: Augmentation of the cardiac natriuretic peptides by beta-receptor antagonism: evidence from a population-based study
AUTHOR(S): Luchner, Andreas; Burnett, John C., Jr.; Jougasaki, Michihisa; Hense, Hans-Werner; Riegger, Gunter A. J.; Schunkert, Heribert
CORPORATE SOURCE: Klinik und Poliklinik fur Innere Medizin II,

University of Regensburg, Regensburg, D-93042, Germany
SOURCE: Journal of the American College of Cardiology (1998), 32(7), 1839-1844
CODEN: JACCDI; ISSN: 0735-1097
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 04 Jan 1999
AB The present retrospective anal. of data derived from a population-based study examined the relationship between intake of β- **receptor antagonists** and plasma concns. of the cardiac natriuretic peptides and their second messenger. β- **Receptor antagonists** are widely used for treatment of cardiovascular disease. In addition to direct effects on heart rate and cardiac contractility, recent evidence suggests that β- **receptor antagonists** may also modulate the cross talk between the sympathetic nervous system and the cardiac natriuretic peptide system. Plasma concns. of atrial natriuretic peptide (ANP), brain natriuretic peptide (BNP) and their second messenger cyclic guanosine monophosphate (**cGMP**) were assessed in addition to anthropometric, hemodynamic and echocardiog. parameters in a population-based sample (n = 672), of which 80 subjects used beta-**receptor antagonists**. Compared to subjects without medication, subjects receiving beta-**receptor antagonists** were characterized by substantially elevated ANP, BNP and **cGMP** plasma concns. (plus 32%, 89% and 18%, resp., $p < 0.01$ each). Anal. of subgroups revealed that this effect was highly consistent and present even in the absence of **hypertension**, left atrial enlargement, left ventricular hypertrophy or left ventricular dysfunction. The most prominent increase was observed in a subgroup with increased left ventricular mass index. By multivariate anal., a statistically significant and independent association between β-receptor antagonism and ANP, BNP and **cGMP** concns. was confirmed. Such an association could not be demonstrated for other antihypertensive agents such as **angiotensin** -converting enzyme inhibitors or diuretics. β- **Receptor antagonists** appear to augment plasma ANP, BNP and **cGMP** concns. The current observation suggests an important contribution of the cardiac natriuretic peptide system to the therapeutic mechanism of beta-**receptor antagonists**.
REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L43 ANSWER 13 OF 16 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:91946 CAPLUS
DOCUMENT NUMBER: 128:191125
TITLE: AT2 receptor stimulation increases aortic cyclic GMP in SHRSP by a kinin-dependent mechanism
AUTHOR(S): Gohlke, Peter; Pees, Christiane; Unger, Thomas
CORPORATE SOURCE: Institute of Pharmacology, Christian-Albrechts University of Kiel and German Institute for High Blood Pressure Research, Heidelberg, Germany
SOURCE: Hypertension (1998), 31(1, Pt. 2), 349-355
CODEN: HPRTDN; ISSN: 0194-911X
PUBLISHER: Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 18 Feb 1998
AB In the present study we tested the hypothesis whether an **angiotensin** AT2 receptor-mediated stimulation of the bradykinin (BK)/nitric oxide (NO) system can account for the effects of AT1 receptor antagonism on aortic **cGMP** described previously in SHRSP. Adult SHRSP were treated for 4 h with **angiotensin** II (ANG II) (30 ng/kg per min i.v.) or vehicle (0.9% NaCl i.v.). Animals were pretreated with vehicle, losartan (100 mg/kg p.o.), PD 123319 (30 mg/kg i.v.), losartan plus PD 123319, icatibant (500 μg/kg i.v.),

NG-nitro-L-arginine Me ester (L-NAME; 1 mg/kg i.v.), or minoxidil (3 mg/kg i.v.). Mean arterial blood pressure (MAP) was continuously monitored over the 4-h exptl. period, and plasma ANG II and aortic **cGMP** were measured by RIA at the end of the study. ANG II infusion over 4 h raised MAP by about 20 mm Hg. Losartan alone or losartan plus ANG II as well as minoxidil plus ANG II markedly reduced blood pressure when compared to vehicle-treated or ANG II-treated animals, resp. Plasma levels of ANG II were increased 2-fold by ANG II infusion alone or by ANG II in combination with icatibant, L-NAME, or minoxidil. The increase in plasma ANG II levels was even more pronounced after losartan treatment. Aortic **cGMP** content was significantly increased by ANG II, losartan, losartan plus ANG II, and minoxidil plus ANG II by 60%, 45%, 68%, and 52%, resp. The effects of ANG II and of losartan plus ANG II on aortic **cGMP** content were both blocked by cotreatment with the AT2 **receptor antagonist** PD 123319. Icatibant and L-NAME abolished the effects of ANG II on aortic **cGMP**. Our results demonstrate the following: (1) ANG II increases aortic **cGMP** by an AT2 receptor-mediated action because the effect could be prevented by an AT2 **receptor antagonist**; (2) the effect of ANG II was not secondary to blood pressure increase because it remained under reduction of MAP with minoxidil; (3) losartan increased aortic **cGMP** most likely by increasing plasma ANG II levels with a subsequent stimulation of AT2 receptor; and (4) the effects of AT2 receptor stimulation are mediated by BK and, subsequently, NO because they were abolished by B2 receptor blockade as well as by NO synthase inhibition.

REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L43 ANSWER 14 OF 16 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1997:24034 CAPLUS

DOCUMENT NUMBER: 126:69912

TITLE: Losartan reduces phenylephrine constrictor response in aortic rings from spontaneously **hypertensive** rats. Role of nitric oxide and angiotensin II type 2 receptors

AUTHOR(S): Maeso, Rosaura; Navarro-Cid, Josefa; Munoz-Garcia, Raquel; Rodrigo, Elena; Ruilope, Luis Miguel; Lahera, Vicente; Cachofeiro, Victoria

CORPORATE SOURCE: School Medicine, Complutense University, Madrid, 28040, Spain

SOURCE: Hypertension (Dallas) (1996), 28(6), 967-972
CODEN: HPRTDN; ISSN: 0194-911X

PUBLISHER: American Heart Association

DOCUMENT TYPE: Journal

LANGUAGE: English

ED Entered STN: 15 Jan 1997

AB Nitric oxide seems to be involved in the mechanisms underlying the antihypertensive and renal responses of losartan in spontaneously **hypertensive** rats (SHR). The authors investigated the contribution of nitric oxide to the effect of this **angiotensin** II (Ang II) type 1 (AT1) **receptor antagonist** on the constrictor response of phenylephrine in aortic rings from SHR. Furthermore, since it has been suggested that Ang II could bind to unblocked AT2 receptors, during administration of an AT1 **receptor antagonist**, the authors also studied the effect of the AT2 **receptor antagonist** PD 123319 on the contractile response to phenylephrine in aortic rings from SHR. To this end, dose-response curves of phenylephrine (10-9 to 10-5 mol/L) in the presence and absence of losartan (10-9, 10-7, and 10-5 mol/L) in SHR aortic rings were studied. Preincubation with losartan reduced the constrictor response to phenylephrine but not to KCl (10 to 120 mmol/L) in a dose-dependent manner. The presence of captopril (10-5 mol/L) in the incubation medium did not alter the response to phenylephrine, even at the dose of 10-3 mol/L. The reduced response to phenylephrine in the presence

of losartan was abolished in both endothelium-denuded rings and rings treated with a nitric oxide synthesis inhibitor. A similar situation was observed in PD 123319-pretreated rings, in which the effect of losartan on the contractile response to phenylephrine was reversed. Losartan was not able to stimulate the production of aortic **cGMP** compared with the control group. Likewise, losartan did not modify the relaxing responses to either acetylcholine or sodium nitroprusside in phenylephrine-preconstricted aortic rings. Furthermore, losartan did not alter isometric tension in aortic rings in either basal or phenylephrine-preconstricted conditions. These data demonstrate that Ang II potentiates the vasoconstriction induced by phenylephrine through the stimulation of AT1 receptors. Moreover, AT2 receptors and nitric oxide appear to be involved in this effect.

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L43 ANSWER 15 OF 16 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:610907 CAPLUS
DOCUMENT NUMBER: 125:265483
TITLE: Cardiac and vascular effects of long-term losartan treatment in stroke-prone spontaneously **hypertensive** rats
AUTHOR(S): Gohlke, Peter; Linz, Wolfgang; Schoelkens, Bernward A.; Wiemer, Gabriele; Unger, Thomas
CORPORATE SOURCE: Department Pharmacology, Christian-Albrechts University Kiel, Kiel, 25601, Germany
SOURCE: Hypertension (Dallas) (1996), 28(3), 397-402
CODEN: HPRTDN; ISSN: 0194-911X
PUBLISHER: American Heart Association
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 14 Oct 1996
AB In previous studies in stroke-prone spontaneously **hypertensive** rats (SHRSP), the authors demonstrated that early-onset, long-term **angiotensin**-converting enzyme inhibitor treatment improved cardiac function and metabolism and increased aortic **cGMP** content even at sub-antihypertensive doses. These effects could be prevented by bradykinin type 2 (B2) receptor blockade with icatibant. In the present study, the authors studied the effects of long-term oral treatment with the **angiotensin** type 1 (AT1) **receptor antagonist** losartan (30 mg/kg per day) on functional and biochem. parameters of the heart and on **cGMP** content in the aorta in SHRSP treated prenatally and subsequently up to the age of 20 wk. Losartan prevented the development of **hypertension** and left ventricular hypertrophy. Cardiac function measured ex vivo in isolated perfused hearts was improved, as demonstrated by significant increases in left ventricular pressure (22.4%), differentiated left ventricular pressure (dP/dtmax) (35.1%), and coronary flow (38%). The release of the intracellular enzymes lactate dehydrogenase and creatine kinase and of lactate into the coronary effluent was reduced by 46.4%, 47.2%, and 63.6%, resp. In myocardial tissue, the concns. of glycogen and the energy-rich phosphates ATP and creatine phosphate were increased by 43.2%, 33.1%, and 42.4%, resp., whereas lactate was decreased by 57.0%. The aortic tissue content of **cGMP** was increased fivefold. The results demonstrate that chronic blockade of AT1 receptors with losartan improved cardiac function and metabolism and increased aortic **cGMP** content in SHRSP to an extent similar to that observed previously after long-term **angiotensin**-converting enzyme inhibitor treatment at a comparably antihypertensive dose. Prevention of **hypertension** and cardiac hypertrophy as well as stimulation of non-AT1 receptors are discussed to explain the cardiac and vascular actions of losartan.

L43 ANSWER 16 OF 16 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:53963 CAPLUS

DOCUMENT NUMBER: 124:164765
TITLE: Chronic low-dose treatment with perindopril improves cardiac function in stroke-prone spontaneously **hypertensive** rats by potentiation of endogenous bradykinin
AUTHOR(S): Gohlke, Peter; Unger, Thomas
CORPORATE SOURCE: Department Pharmacology, Christian Albrechts University Kiel, Kiel, 424105, Germany
SOURCE: American Journal of Cardiology (1995), 76(15), 41E-5E
CODEN: AJCDAG; ISSN: 0002-9149
PUBLISHER: Excerpta Medica
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 26 Jan 1996
AB The authors investigated the effect of chronic **angiotensin** -converting enzyme (ACE) inhibitor treatment on functional and biochem. cardiac parameters in stroke-prone spontaneously **hypertensive** rats (SHRsp). Animals were treated prenatally and, subsequently, up to the age of 20 wk with the ACE inhibitor perindopril (0.01 and 1 mg/kg per day). The contribution of endogenous bradykinin potentiation to the actions of the ACE inhibitor was assessed by co-treatment with the bradykinin B2-**receptor antagonist**, icatibant (500 μg/kg/day s.c.), from 6 to 20 wk of age and by measurement of myocardial prostacyclin and **cGMP** concns. Chronic high-dose treatment with perindopril attenuated the development of **hypertension** and left ventricular hypertrophy while low-dose perindopril treatment had no effect on these parameters. However, low-dose perindopril improved cardiac function of isolated perfused hearts as demonstrated by an increasing left ventricular pressure and dp/dtmax without change in heart rate. Low-dose perindopril further reduced lactate concns. and the enzymic activities of lactate dehydrogenase and creatine kinase in the coronary venous effluent and increased tissue concns. of glycogen, ATP, and creatine kinase in the myocardium. Concomitant chronic bradykinin receptor blockade abolished all ACE inhibitor-induced effects on cardiac function and metabolism Cardiac prostacyclin concns. were 3-fold elevated in perindopril-treated animals when compared to vehicle-treated controls, while cardiac **cGMP** concns. remained unchanged. The data demonstrate that chronic ACE inhibitor treatment can improve cardiac function and metabolism independently of the antihypertensive and antihypertrophic drug actions by potentiation of endogenous bradykinin.

=> d his

(FILE 'HOME' ENTERED AT 11:49:08 ON 02 MAR 2005)

FILE 'CAPLUS' ENTERED AT 11:49:13 ON 02 MAR 2005
E FOX DAVID/AU
L1 69 S E2-E3, E20-E22
E HUGHES BERNADETTE/AU
L2 22 S E3-E4
E HUGHES B/AU
L3 40 S E3
E FOX D/AU
E FOX D?/AU
E FOX D/AU
L4 75 S E3
L5 144 S L1 OR L4
L6 62 S L2 OR L3
L7 204 S L5 OR L6
L8 10 S L7 AND HYPERTENSI?
L9 0 S L7 AND (CYCLIC GUANOSINE MONOPHOSPHATE (W) (PHOSPHODIESTERASE
L10 6 S L7 AND ("CGMP" OR "PDE5" OR "ANGIOTENSIN II RECEPTOR ANTAGONI

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FILE 'REGISTRY' ENTERED AT 11:57:43 ON 02 MAR 2005
                E SILDENAFIL/CN
L11           2 S E3-E4
                E TADALAFIL/CN
L12           1 S E3
                E VARDENAFIL/CN
L13           3 S E3-E5
L14           1 S CANDESARTAN/CN
                E CANDESARTAN/CN
L15           2 S E3-E5
                E EPROSARTAN/CN
L16           2 S E3-E5
                E IRBESARTAN/CN
L17           4 S E3-E6
                E LOSARTAN/CN
L18           4 S E3-E7
                E OLMESARTAN/CN
L19           2 S E3-E5
                E SARALASIN/CN
L20           2 S E3-E4
                E TELMISARTAN/CN
L21           5 S E3-E7
                E VALSARTAN/CN
L22           2 S E3-E4
L23           6 S L11 OR L12 OR L13
L24          23 S L15 OR L16 OR L17 OR L18 OR L19 OR L20 OR L21 OR L22

     FILE 'CAPLUS' ENTERED AT 12:02:01 ON 02 MAR 2005
L25        1081 S L23
L26        4320 S L24
                E HYPERTENSION/BI
L27       78751 S E3, E16
                E HYPERTENSION/CT
L28       43383 S E3
L29       78751 S L27 OR L28
L30       80818 S L29 OR (HIGH BLOOD PRESSURE) OR (ELEVATED BLOOD PRESSURE) OR
L31          36 S L25 AND L26
L32           9 S L31 (L) L30
L33           9 S L30 AND L31
L34          34 S L25 (L) L30
L35        1025 S L26 (L) L30
L36           0 S L34 AND L35
L37           9 S L31 AND HYPERTENS?
L38           0 S L37 NOT L33
L39       20335 S "CGMP" OR "PDE5" OR (CYCLIC GUANOSINE MONOPHOSPHATE (W) PHOSP
L40        6539 S (ANGIOTENSIN (L) RECEPTOR ANTAGONIST) OR (ANGIOTENSIN RECEPTO
L41          80 S L39 (L) L40
L42          17 S L41 AND HYPERTENS?
L43          16 S L42 NOT L33

=> d cost
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
CONNECT CHARGES                                         8.58      16.78
NETWORK CHARGES                                         1.32       2.64
SEARCH CHARGES                                         56.70     254.68
DISPLAY CHARGES                                        66.25     108.65
                                                      -------   -------
FULL ESTIMATED COST                                   132.85     382.75

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                       ENTRY    SESSION
CA SUBSCRIBER PRICE                                   -18.25     -29.93
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IN FILE 'CAPLUS' AT 12:15:29 ON 02 MAR 2005

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=> s l31 or l41
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         25215 STROKE?
        109357 DIABET?
          6780 CONGESTIVE
        300773 HEART
         26101 HEARTS
        302455 HEART
                 (HEART OR HEARTS)
        174094 FAILURE?
          6178 CONGESTIVE HEART FAILURE?
                 (CONGESTIVE(W)HEART(W)FAILURE?)
L45          15 L44 AND (ANGINA? OR STROKE? OR DIABET? OR CONGESTIVE HEART FAILU
                RE?)

=> s l45 not l43
L46          11 L45 NOT L43

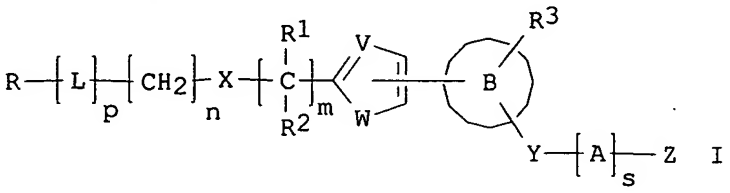
=> s l46 not l33
L47           6 L46 NOT L33

=> d l47 1-6 ibib ed abs

L47  ANSWER 1 OF 6  CAPLUS  COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:         2004:878382  CAPLUS
DOCUMENT NUMBER:          141:350161
TITLE:                    Preparation of azole compounds as PTP1B inhibitors
INVENTOR(S):              Ikemoto, Tomoyuki; Tanaka, Masahiro; Yuno, Takeo;
                          Sakamoto, Johei; Nakanishi, Hiroyuki; Nakagawa,
                          Yuichi; Ohta, Takeshi; Sakata, Shohei; Morinaga,
                          Hisayo
PATENT ASSIGNEE(S):       Japan Tobacco Inc., Japan
SOURCE:                   PCT Int. Appl., 542 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 Japanese
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.          DATE
     ---------------      ----   --------    --------------------     --------
     WO 2004089918         A1    20041021    WO 2004-JP5119           20040409
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
             LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
             NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
             TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
             BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE,
             ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI,
             SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN,
             TD, TG
PRIORITY APPLN. INFO.:                        JP 2003-105267       A  20030409
                                              JP 2003-157590       A  20030603
OTHER SOURCE(S):          MARPAT 141:350161
ED   Entered STN:  22 Oct 2004
```

GI



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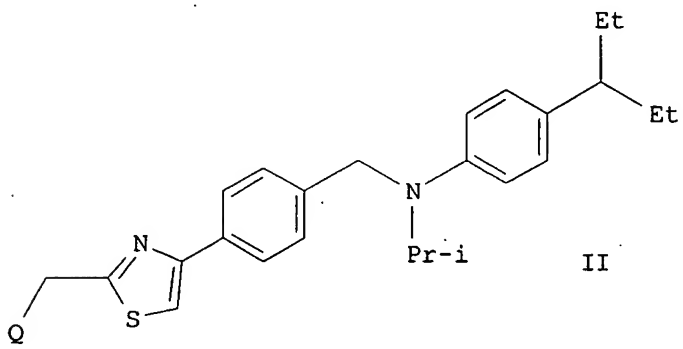

II

AB Title compds. I [V = N, CH; W = S, O; m = 0-2; R1, R2 = H, alkyl; X = NR4, etc.; R4 = H, alkyl; n = 0-4; p = 0, 1; L = CR20R21, etc.; R20 = H, alkyl, etc.; R21 = H, alkyl, etc.; R = CO2R19, etc.; R19 = H, alkyl; B = aryl, heteroaryl; R3 = H, halo, etc.; Y = O, etc.; s = 0, 1; A = (un)substituted alkylene with cycloalkyl; Z = cycloalkyl, etc.] were prepared For example, O-alkylation of 5-hydroxynicotinic acid Me ester with compound II [Q = Cl], e.g., prepared from 4-bromoacetylbenzoic acid in 5 steps, followed by saponification
afforded compound II [3-carboxypyridin-5-yloxy] in 44.1% overall yield. In PTP1B (protein tyrosine phosphatase 1B) inhibition assays, the IC50 value of compound II [Q = 3-carboxypyridin-5-yloxy] was 0.28 μM. Compds. I are claimed useful for the treatment of obesity, **diabetes**, etc.
Formulations are given.

REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L47 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:154230 CAPLUS
DOCUMENT NUMBER: 138:210277
TITLE: Synthesis and use of reagents for improved DNA lipofection and/or slow release prodrug and drug therapies
INVENTOR(S): Diamond, Scott L.; Gruneich, Jeffrey
PATENT ASSIGNEE(S): The Trustees of the University of Pennsylvania, USA
SOURCE: PCT Int. Appl., 70 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003015757	A1	20030227	WO 2002-US26152	20020815

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,

CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

EP 1424998 A1 20040609 EP 2002-759383 20020815

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK

PRIORITY APPLN. INFO.: US 2001-312729P P 20010816
US 2002-358138P P 20020220
WO 2002-US26152 W 20020815

ED Entered STN: 28 Feb 2003

AB The invention relates to compns. and methods for a one-step synthetic technique for making cationic steroid or cationic drug mols. for use as delivery vehicles. The invention further relates to methods for using cationic steroid mols. in lipofection or transfection, delivery of drugs, and for treatment of inflamrnation and other diseases and disorders. The invention also relates to cationic steroid prodrugs and cationic prodrugs and to methods of modifying drugs.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L47 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:431177 CAPLUS

DOCUMENT NUMBER: 135:162931

TITLE: Angiotensin regulates endothelin-B receptor in rat inner medullary collecting duct

AUTHOR(S): Wong, Norman L. M.; Tsui, Joseph K. C.

CORPORATE SOURCE: Department of Medicine, University of British Colombia, Vancouver, BC, Can.

SOURCE: Metabolism, Clinical and Experimental (2001), 50(6), 661-666
CODEN: METAAJ; ISSN: 0026-0495

PUBLISHER: W. B. Saunders Co.

DOCUMENT TYPE: Journal

LANGUAGE: English

ED Entered STN: 14 Jun 2001

AB The authors' recent studies showed that endothelin (ET)B receptors are downregulated in **congestive heart failure**. These changes in ETB receptor d. can be prevented by **angiotensin** -converting enzyme inhibitors, suggesting a possible role for **angiotensin**. Using isolated inner medullary collecting ducts (IMCD), the authors examined the possibility that **angiotensin** -induced downregulation of ETB receptors is accompanied by a decrease in ETB receptor mRNA. Binding studies showed that overnight incubation with **angiotensin** II induced a downregulation of ETA and ETB receptors' d. in IMCD by 39% and 29%, resp. This downregulation in ET receptor d. was abolished when IMCD was coincubated with **angiotensin** II and its **receptor antagonist** saralasin. Furthermore, when the cells were exposed to phorbol myristate acetate (PMA), it resulted in a reduction in ETA and ETB receptor binding sites by 41% and 34%, resp., suggesting the involvement of protein kinase C (PKC). In isolated IMCD, ET-1 induced an increase in cyclic guanosine monophosphate (**cGMP**) accumulation (705 ± 63 to 1,015 ± 88 fmol/μg protein/5min, P < .01), and the ET-1-induced accumulation was attenuated in the presence of **angiotensin** II (641 ± 45 to 809 ± 46 fmol/μg protein/5min, P < .01). Using competitive PCR method, the authors also observed downregulation of ETA and ETB receptors mRNA in IMCD treated with **angiotensin** II (ETA, 1.09±0.11 v 0.77 ± 0.07 amol/μg of

total RNA, P < .01; ETB, 14.80 ± 1.95 v 8.65 ± 0.67 amol/μg of total RNA, P < .01). The addition of a PKC inhibitor abolished the downregulation of ETA and ETB receptor mRNA induced by **angiotensin** II (ETA, 1.25 ± 0.07 v 1.19 ± 0.06 amol/μg of total RNA, not significant [NS]; ETB, 14.36 ± 0.83 to 13.68 ± 0.64 amol/μg of total RNA, NS). These results suggest that **angiotensin** II-induced downregulation of ETA and ETB receptors mRNA is mediated by a mechanism involving PKC.

REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L47 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2000:204037 CAPLUS
DOCUMENT NUMBER: 132:216831
TITLE: Angiotensin II type 1 receptor antagonist decreases plasma levels of tumor necrosis factor alpha, interleukin-6 and soluble adhesion molecules in patients with chronic heart failure
AUTHOR(S): Tsutamoto, Takayoshi; Wada, Atsuyuki; Maeda, Keiko; Mabuchi, Naoko; Hayashi, Masaru; Tsutsui, Takashi; Ohnishi, Masato; Sawaki, Masahide; Fujii, Masanori; Matsumoto, Takehiro; Kinoshita, Masahiko
CORPORATE SOURCE: First Department of Internal Medicine, Shiga University of Medical Science, Otsu, Japan
SOURCE: Journal of the American College of Cardiology (2000), 35(3), 714-721
CODEN: JACCDI; ISSN: 0735-1097
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 30 Mar 2000
AB OBJECTIVES: To evaluate the effects of an **angiotensin** (Ang II) type 1 **receptor antagonist** on immune markers in patients with **congestive heart failure** (CHF). BACKGROUND: Ang II stimulates production of immune factors via the Ang II type 1 receptor in vitro, and the long-term effects of Ang II type 1 **receptor antagonists** on plasma markers of immune activation are unknown in patients with CHF. METHODS: Twenty-three patients with mild to moderate CHF with left ventricular dysfunction were randomly divided into two groups: treatment with Ang II type 1 receptor (candesartan cilexetil) (n = 14) or placebo (n = 9). We measured plasma levels of immune factors such as tumor necrosis factor alpha (TNFalpha), interleukin-6 (IL-6), soluble intercellular adhesion mol.-1 (sICAM-1) and soluble vascular cell adhesion mol.-1 (sVCAM-1). We also measured plasma levels of the neurohumoral factors such as atrial natriuretic peptide (ANP) and brain natriuretic peptide (BNP) and **cGMP** (**cGMP**), a biol. marker of ANP and BNP. RESULTS: Plasma levels of TNFalpha, IL-6, sICAM-1 and sVCAM-1 were increased in the 23 CHF patients compared with normal subjects and significantly decreased after 14 wk of candesartan cilexetil treatment, but did not change in the placebo group. Plasma levels of BNP, which is a marker of ventricular injury, significantly decreased, and the molar ratio of plasma **cGMP** to cardiac natriuretic peptides (ANP + BNP) was significantly increased after candesartan cilexetil treatment, but did not change in the placebo group. CONCLUSIONS: These findings suggest that 14 wk of treatment with an Ang II type 1 **receptor antagonist** (candesartan cilexetil) decreased plasma levels of the immune markers such as TNFalpha, IL-6, sICAM-1 and sVCAM-1 and that it improved the biol. compensatory action of endogenous cardiac natriuretic peptides in patients with mild to moderate CHF.

REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L47 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1997:778166 CAPLUS
DOCUMENT NUMBER: 128:60216
TITLE: Impaired nitric oxide-mediated renal vasodilation in rats with experimental heart failure; role of angiotensin II
AUTHOR(S): Abassi, Zaid A.; Gurbanov, Konstantin; Mulroney, Susan E.; Potlog, Clariss; Opgenorth, Terry J.; Hoffman, Aaron; Haramati, Aviad; Winaver, Joseph
CORPORATE SOURCE: Department of Physiology and Biophysics, Faculty of Medicine, Technion, Haifa, Israel
SOURCE: Circulation (1997), 96(10), 3655-3664
CODEN: CIRCAZ; ISSN: 0009-7322
PUBLISHER: American Heart Association
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 13 Dec 1997
AB **Congestive heart failure** (CHF) is associated with a decrease in renal perfusion. Because endothelium-derived NO is important in the regulation of renal blood flow (RBF), the authors tested the hypothesis that an impairment in the NO system may contribute to the decrease in RBF in rats with exptl. CHF. Studies were performed in rats with exptl. high-output CHF induced by aortocaval (AV) fistula and sham-operated controls. In controls, incremental doses of acetylcholine (ACh, 1 to 100 μg/kg/min) increased RBF and caused a dose-related decrease in renal vascular resistance (RVR). However, the increase in RBF and decrease in RVR were markedly attenuated in rats with CHF. Likewise, the effects of ACh on urinary sodium and **cGMP** excretion were also diminished in CHF rats, as was the renal vasodilatory effect of the NO donor S-nitroso-N-acetylpenicillamine (SNAP). These attenuated responses to endothelium-dependent and -independent renal vasodilators in CHF rats occurred despite a normal baseline and stimulated NO2+NO3 excretion and normal expression of renal endothelial NO synthase (eNOS), as determined by eNOS mRNA levels and immunoreactive protein. Infusion of the NO precursor L-arginine did not affect baseline RBF or the response to ACh in rats with CHF. However, administration of the nonpeptide **angiotensin II receptor antagonist** A81988 before ACh completely restored the renal vasodilatory response to ACh in CHF rats. This study demonstrates that despite a significant attenuation in the NO-related renal vasodilatory responses, the integrity of the renal NO system is preserved in rats with chronic AV fistula. This impairment in NO-mediated renal vasodilation in exptl. CHF appears to be related to increase activity of the renin-**angiotensin** system and may contribute further to the decrease in renal perfusion seen in CHF.
REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L47 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:351367 CAPLUS
DOCUMENT NUMBER: 127:63989
TITLE: Chronic effects of ANG II antagonist in heart failure: improvement of cGMP generation from ANP
AUTHOR(S): Maeda, Yukiharu; Wada, Atsuyuki; Tsutamoto, Takayoshi; Fukai, Daisuke; Kinoshita, Masahiko
CORPORATE SOURCE: First Department of Internal Medicine, Shiga University of Medical Science, Ohtsu, 520-21, Japan
SOURCE: American Journal of Physiology (1997), 272(5, Pt. 2), H2139-H2145
CODEN: AJPHAP; ISSN: 0002-9513
PUBLISHER: American Physiological Society
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 05 Jun 1997
AB To evaluate the effects of endogenous **angiotensin** II (ANG II) on the development of **congestive heart failure**

(CHF), we examined cardiorenal and hormonal factors after chronic administration of the ANG II type 1 **receptor antagonist** TCV-116 in dogs with CHF induced by rapid right ventricular pacing. After 8 days of pacing, TCV-116 administration [1 (group 1) or 3 mg·kg-1·day-1 (group 2)] was started and continued until the 22nd day. TCV-116 was found to have protected the deterioration of cardiorenal functions and the activation of neurohormonal factors. Although there was no significant difference in the pulmonary capillary wedge pressure or plasma atrial natriuretic peptide (ANP) level between the TCV-116-treated groups (354 ± 85 and 364 ± 29 pg/mL for groups 1 and 2, resp.) and the vehicle group (385 ± 20 pg/mL), the plasma guanosine 3',5'-cyclic monophosphate (**cGMP**) levels, a second messenger of ANP, were twofold higher in TCV-116-treated groups (49.4 ± 10.2 and 50.6 ± 7.7 pmol/mL for groups 1 and 2, resp.) than in the vehicle group (24 ± 4.0 pmol/mL), with a high correlation between the plasma ANP and **cGMP** levels ($r = 0.90$; $P < 0.05$). These findings indicate that endogenous ANG II has important roles in hemodynamics and renal functions during the development of CHF, which may be due, in part, to a reduction in endogenous ANP activity, suggesting the usefulness of an ANG II-**receptor antagonist** against the development of CHF.

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d his

(FILE 'HOME' ENTERED AT 11:49:08 ON 02 MAR 2005)

FILE 'CAPLUS' ENTERED AT 11:49:13 ON 02 MAR 2005

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                E HUGHES BERNADETTE/AU
L2           22 S E3-E4
                E HUGHES B/AU
L3           40 S E3
                E FOX D/AU
                E FOX D?/AU
                E FOX D/AU
L4           75 S E3
L5          144 S L1 OR L4
L6           62 S L2 OR L3
L7          204 S L5 OR L6
L8           10 S L7 AND HYPERTENSI?
L9            0 S L7 AND (CYCLIC GUANOSINE MONOPHOSPHATE (W) (PHOSPHODIESTERASE
L10           6 S L7 AND ("CGMP" OR "PDE5" OR "ANGIOTENSIN II RECEPTOR ANTAGONI
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FILE 'REGISTRY' ENTERED AT 11:57:43 ON 02 MAR 2005

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L11           2 S E3-E4
                E TADALAFIL/CN
L12           1 S E3
                E VARDENAFIL/CN
L13           3 S E3-E5
L14           1 S CANDESARTAN/CN
                E CANDESARTAN/CN
L15           2 S E3-E5
                E EPROSARTAN/CN
L16           2 S E3-E5
                E IRBESARTAN/CN
L17           4 S E3-E6
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L18           4 S E3-E7
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L19           2 S E3-E5
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L20             2 S E3-E4
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                E VALSARTAN/CN
L22             2 S E3-E4
L23             6 S L11 OR L12 OR L13
L24            23 S L15 OR L16 OR L17 OR L18 OR L19 OR L20 OR L21 OR L22

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L26          4320 S L24
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L27         78751 S E3, E16
                E HYPERTENSION/CT
L28         43383 S E3
L29         78751 S L27 OR L28
L30         80818 S L29 OR (HIGH BLOOD PRESSURE) OR (ELEVATED BLOOD PRESSURE) OR
L31            36 S L25 AND L26
L32             9 S L31 (L) L30
L33             9 S L30 AND L31
L34            34 S L25 (L) L30
L35          1025 S L26 (L) L30
L36             0 S L34 AND L35
L37             9 S L31 AND HYPERTENS?
L38             0 S L37 NOT L33
L39         20335 S "CGMP" OR "PDE5" OR (CYCLIC GUANOSINE MONOPHOSPHATE (W) PHOSP
L40          6539 S (ANGIOTENSIN (L) RECEPTOR ANTAGONIST) OR (ANGIOTENSIN RECEPTO
L41            80 S L39 (L) L40
L42            17 S L41 AND HYPERTENS?
L43            16 S L42 NOT L33
L44           115 S L31 OR L41
L45            15 S L44 AND (ANGINA? OR STROKE? OR DIABET? OR CONGESTIVE HEART FA
L46            11 S L45 NOT L43
L47             6 S L46 NOT L33

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L48             5 L46 NOT L47

=> d l48 1-5 ibib ed abs

L48  ANSWER 1 OF 5  CAPLUS  COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:         2005:77981  CAPLUS
DOCUMENT NUMBER:          142:162662
TITLE:                    Nanoparticulate glipizide compositions
INVENTOR(S):              Bosch, H. William; Ryde, Niels P.
PATENT ASSIGNEE(S):       Elan Pharma International Limited, USA
SOURCE:                   U.S. Pat. Appl. Publ., 24 pp., Cont.-in-part of U.S.
                          Ser. No. 276,400.
                          CODEN: USXXCO
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   16
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.          DATE
     ---------------      ----   --------    --------------------     --------
     US 2005019412         A1    20050127    US 2003-701064           20031105
     US 2002012675         A1    20020131    US 1999-337675           19990622
     WO 2001087264         A2    20011122    WO 2001-US15983          20010518
     WO 2001087264         A3    20020620
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
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LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT,
RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US,
UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 2004013613	A1	20040122	US 2003-276400		20030115
PRIORITY APPLN. INFO.:			US 1998-164351	B2	19981001
			US 1999-337675	A2	19990622
			WO 2001-US15983	W	20010518
			US 2003-276400	A2	20030115
			US 2000-572961	A	20000518

ED Entered STN: 28 Jan 2005

AB The present invention is directed to nanoparticulate compns. comprising glipizide. The glipizide particles of the composition preferably have an effective average particle size of <2 μ. Thus, a formulation contained spray-dried glipizide 5.33, mannitol 13.47, xylitol 40.53, citric acid 19.60, sodium bicarbonate 19.33, Asparatme 0.28, PEG-4000 0.93, and sodium stearyl fumarate 0.53%.

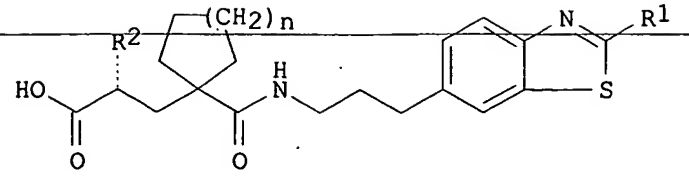
L48 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:759835 CAPLUS
DOCUMENT NUMBER: 141:277616
TITLE: Preparation of 3-(1-[3-(1,3-benzothiazol-6-yl)propylcarbamoyl]cycloalkyl)propanoic acid derivatives as nep inhibitors
INVENTOR(S): Hepworth, David
PATENT ASSIGNEE(S): Pfizer Inc., UK
SOURCE: U.S. Pat. Appl. Publ., 27 pp., which
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004180941	A1	20040916	US 2004-800065	20040312
WO 2004080985	A1	20040923	WO 2004-IB822	20040309

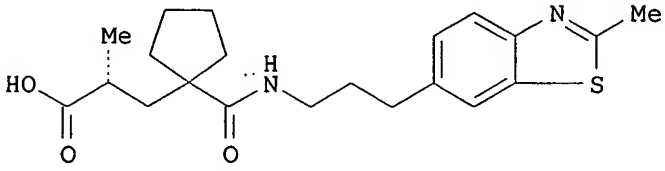
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE,
ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI,
SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN,
TD, TG

NL 1025709	A1	20040916	NL 2004-1025709		20040312
PRIORITY APPLN. INFO.:			GB 2003-5916	A	20030314
			US 2003-464608P	P	20030422
			GB 2003-29143	A	20031216
			US 2004-538079P	P	20040120

OTHER SOURCE(S): MARPAT 141:277616
ED Entered STN: 17 Sep 2004
GI



I



II

AB The invention relates to the use of title compds. I [R1 = H or Me; R2 = Me or Et; n = 1 or 2] as inhibitors of neutral endopeptidase enzyme (NEP), processes for the preparation thereof, intermediates used in the preparation thereof and compns. containing said inhibitors. Thus, e.g., II was prepared by amidation of 1-[(2R)-3-tert-butoxy-2-methyl-3-oxopropyl]cyclopentane carboxylic acid with 3-(2-methyl-1,3-benzothiazol-6-yl)propylamine dihydrochloride (preparation given) with subsequent hydrolysis to provide the free acid. I have been demonstrated to possess IC50 values of <20 nanomolar in tests for NEP inhibition and demonstrate a selectivity over soluble secreted endopeptidase (SEP) of at least 1000 fold. These inhibitors have utility in a variety of therapeutic areas including the treatment of male and female sexual dysfunction, particularly female sexual dysfunction (FSD), especially wherein the FSD is female sexual arousal disorder (FSAD).

L48 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:269863 CAPLUS
DOCUMENT NUMBER: 140:281417
TITLE: Combination therapy using antihypertensive agents and endothelin antagonists for vascular conditions associated with a male or female sexual dysfunction
INVENTOR(S): Adams, Michael A.; Hale, Taben M.; Heaton, Jeremy P. W.
PATENT ASSIGNEE(S): Queen's University At Kingston, Can.; Callegy Pharmaceuticals, Inc.
SOURCE: U.S. Pat. Appl. Publ., 29 pp., Cont.-in-part of U.S. Pat. Appl. 2003 8,020.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004063719	A1	20040401	US 2003-429197	20030502
US 6284763	B1	20010904	US 1999-382749	19990825
US 2002035067	A1	20020321	US 2001-902787	20010712
US 6458797	B2	20021001		
US 2003008020	A1	20030109	US 2002-192281	20020709
US 6787553	B2	20040907		
US 2004234619	A1	20041125	US 2004-869755	20040615

PRIORITY APPLN. INFO.:

US 1998-98178P	P	19980826
US 1999-382749	A1	19990825
US 2001-902787	A1	20010712
US 2002-377917P	P	20020502

US 2002-192281 A2 20020709

ED Entered STN: 02 Apr 2004

AB The present invention provides a method for a more efficacious treatment of a vascular condition through the administration of a therapeutically effective amount of a combination of an anti-pressor agent, an endothelin antagonist, and a sex hormone for repetitive cycles of on/off-treatment. In one embodiment, the invention provides a method for the prevention of tolerance induced by an anti-pressor agent via the inclusion of an endothelin antagonist in a combination therapy approach to remodel vascular structure and treat vascular conditions associated with a male or female sexual dysfunction, atherosclerosis, renal failure, hypertension, **congestive heart failure, diabetic** nephropathy, and **diabetic** neuropathy. The anti-pressor agent comprises one or more compds. such as prostaglandin-E 1 , an ACE inhibitor, an angiotensin-II receptor antagonist, an α1-adrenergic receptor antagonist, a β-adrenergic receptor antagonist, a calcium channel blocker, an activator of guanylyl cyclase or adenyl cyclase, a phosphodiesterase inhibitor, and hydralazine. The endothelin antagonist comprises one or more compds. such as a peptidal endothelin antagonist, a non-peptidal endothelin antagonist, and an inhibitor of endothelin converting enzyme. Such a combination therapy approach enhances the efficacy of the anti-pressor agent and enables an increase in the frequency and duration of anti-pressor administrations for the long term treatment of vascular conditions.

L48 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:60341 CAPLUS

DOCUMENT NUMBER: 140:117406

TITLE: Liquid dosage compositions of stable nanoparticulate drugs

INVENTOR(S): Bosch, William H.; Hilborn, Matthew R.; Hovey, Douglas C.; Kline, Laura J.; Lee, Robert W.; Pruitt, John D.; Ryde, Niels P.; Ryde, Tuula A.; Xu, Shuqian

PATENT ASSIGNEE(S): Elan Pharma International, Ltd, Ire.

SOURCE: PCT Int. Appl., 68 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 16

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004006959	A1	20040122	WO 2003-US22187	20030716

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2002-396530P P 20020716

ED Entered STN: 26 Jan 2004

AB The present invention relates to liquid dosage compns. of stable nanoparticulate drugs. The liquid dosage compns. of the invention include osmotically active crystal growth inhibitors that stabilize the nanoparticulate active agents against crystal and particle size growth of the drug. Thus, an aqueous nanoparticulate colloidal dispersion (NCD) comprising drug 32.5 Copovidone 6.5, and dioctyl sodium sulfosuccinate 0.464% by weight was prepared by milling for 3.8 h under high energy milling conditions. The final mean particle size (by weight) of the drug particles

was 161 nm. The concentrated NCD was then diluted with preserved water and glycerol (the osmotically active crystal growth inhibitor) to 0.5-3.0% drug.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L48 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:396889 CAPLUS
DOCUMENT NUMBER: 138:401744
TITLE: Preparation of polycyclic guanine derivative phosphodiesterase V inhibitors
INVENTOR(S): Asberom, Theodros; Clader, John W.; Hu, Yueqing; Pissarnitski, Dmitri A.; Stamford, Andrew W.; Xu, Ruo
PATENT ASSIGNEE(S): Schering Corporation, USA
SOURCE: PCT Int. Appl., 95 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003042216	A1	20030522	WO 2002-US35721	20021107
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MA, MD, MG, MK, MN, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SC, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UZ, VC, VN, YU, ZA, ZM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003176413	A1	20030918	US 2002-290011	20021107
EP 1442042	A1	20040804	EP 2002-786685	20021107
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				

PRIORITY APPLN. INFO.:	US 2001-344498P	P	20011109
	WO 2002-US35721	W	20021107

OTHER SOURCE(S): MARPAT 138:401744
ED Entered STN: 23 May 2003
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [q = 0-2; R1, R3-6 = H, alkyl, aryl, heteroaryl, cycloalkyl, heterocycloalkyl; R2 = H, halo, alkyl, alkoxy, etc.; Y = alkyl, aryl] are prepared For instance, 4-amino-1-benzyl-5-(ethoxycarbonyl)imidazole (preparation given) is treated with ethylisocyanate (o-xylene, reflux, 16 h), the resulting product cyclized (MeOH, NaOMe, reflux, 4 h), subsequently treated with POCl3 and the product used to alkylate (R)-2-amino-3-phenylpropanol (NMP, 130°, 12 h) which provides II. II is treated with MsCl (Et3N), debenzylated (MeOH, NH4O2CH, Pd(OH)2/C, reflux, 3 h), brominated (HOAc, NaOAc, Br2), alkylated with 3-chloro-4-methoxybenzyl bromide (DMF, K2CO3) and treated with NaOEt (DMF/EtOH) to afford III. III has IC50 < 4.1 nM for PDE V and IC50 > 300 nM for PDE VI. I are useful for treating sexual dysfunction.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

```
=> d cost
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY     SESSION
CONNECT CHARGES                                            10.92       19.12
NETWORK CHARGES                                             1.68        3.00
SEARCH CHARGES                                             68.04      266.02
DISPLAY CHARGES                                            95.40      137.80
                                                          -------     -------
FULL ESTIMATED COST                                       176.04      425.94

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)              SINCE FILE      TOTAL
                                                           ENTRY     SESSION
CA SUBSCRIBER PRICE                                       -26.28      -37.96

IN FILE 'CAPLUS' AT 12:19:01 ON 02 MAR 2005


=> d his

     (FILE 'HOME' ENTERED AT 11:49:08 ON 02 MAR 2005)

     FILE 'CAPLUS' ENTERED AT 11:49:13 ON 02 MAR 2005
                E FOX DAVID/AU
L1           69 S E2-E3, E20-E22
                E HUGHES BERNADETTE/AU
L2           22 S E3-E4
                E HUGHES B/AU
L3           40 S E3
                E FOX D/AU
                E FOX D?/AU
                E FOX D/AU
L4           75 S E3
L5          144 S L1 OR L4
L6           62 S L2 OR L3
L7          204 S L5 OR L6
L8           10 S L7 AND HYPERTENSI?
L9            0 S L7 AND (CYCLIC GUANOSINE MONOPHOSPHATE (W) (PHOSPHODIESTERASE
L10           6 S L7 AND ("CGMP" OR "PDE5" OR "ANGIOTENSIN II RECEPTOR ANTAGONI

     FILE 'REGISTRY' ENTERED AT 11:57:43 ON 02 MAR 2005
                E SILDENAFIL/CN
L11           2 S E3-E4
                E TADALAFIL/CN
L12           1 S E3
                E VARDENAFIL/CN
L13           3 S E3-E5
L14           1 S CANDESARTAN/CN
                E CANDESARTAN/CN
L15           2 S E3-E5
                E EPROSARTAN/CN
L16           2 S E3-E5
                E IRBESARTAN/CN
L17           4 S E3-E6
                E LOSARTAN/CN
L18           4 S E3-E7
                E OLMESARTAN/CN
L19           2 S E3-E5
                E SARALASIN/CN
L20           2 S E3-E4
                E TELMISARTAN/CN
L21           5 S E3-E7
                E VALSARTAN/CN
L22           2 S E3-E4
L23           6 S L11 OR L12 OR L13
```

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L24          23 S L15 OR L16 OR L17 OR L18 OR L19 OR L20 OR L21 OR L22
```

```
     FILE 'CAPLUS' ENTERED AT 12:02:01 ON 02 MAR 2005
L25        1081 S L23
L26        4320 S L24
                E HYPERTENSION/BI
L27       78751 S E3, E16
                E HYPERTENSION/CT
L28       43383 S E3
L29       78751 S L27 OR L28
L30       80818 S L29 OR (HIGH BLOOD PRESSURE) OR (ELEVATED BLOOD PRESSURE) OR
L31          36 S L25 AND L26
L32           9 S L31 (L) L30
L33           9 S L30 AND L31
L34          34 S L25 (L) L30
L35        1025 S L26 (L) L30
L36           0 S L34 AND L35
L37           9 S L31 AND HYPERTENS?
L38           0 S L37 NOT L33
L39       20335 S "CGMP" OR "PDE5" OR (CYCLIC GUANOSINE MONOPHOSPHATE (W) PHOSP
L40        6539 S (ANGIOTENSIN (L) RECEPTOR ANTAGONIST) OR (ANGIOTENSIN RECEPTO
L41          80 S L39 (L) L40
L42          17 S L41 AND HYPERTENS?
L43          16 S L42 NOT L33
L44         115 S L31 OR L41
L45          15 S L44 AND (ANGINA? OR STROKE? OR DIABET? OR CONGESTIVE HEART FA
L46          11 S L45 NOT L43
L47           6 S L46 NOT L33
L48           5 S L46 NOT L47

=> file medline biosis embase wpids
COST IN U.S. DOLLARS                            SINCE FILE      TOTAL
                                                   ENTRY    SESSION
FULL ESTIMATED COST                                176.49     426.39

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)      SINCE FILE      TOTAL
                                                   ENTRY    SESSION
CA SUBSCRIBER PRICE                                -26.28     -37.96

FILE 'MEDLINE' ENTERED AT 12:19:37 ON 02 MAR 2005

FILE 'BIOSIS' ENTERED AT 12:19:37 ON 02 MAR 2005
Copyright (c) 2005 The Thomson Corporation

FILE 'EMBASE' ENTERED AT 12:19:37 ON 02 MAR 2005
COPYRIGHT (C) 2005 Elsevier Inc. All rights reserved.

FILE 'WPIDS' ENTERED AT 12:19:37 ON 02 MAR 2005
COPYRIGHT (C) 2005 THE THOMSON CORPORATION

=> s (sildenafil? or viagra? or tadalafil? or "IC-351" or "IC 351" or "IC351" or
cialis? or vardenafil? or levitra?_
UNMATCHED LEFT PARENTHESIS '(SILDENAFIL'
The number of right parentheses in a query must be equal to the
number of left parentheses.

=> s (sildenafil? or viagra? or tadalafil? or "IC-351" or "IC 351" or "IC351" or
cialis? or vardenafil? or levitra?_)
L49        7998 (SILDENAFIL? OR VIAGRA? OR TADALAFIL? OR "IC-351" OR "IC 351"
                OR "IC351" OR CIALIS? OR VARDENAFIL? OR LEVITRA?_)

=> s (sildenafil? or viagra? or tadalafil? or "IC-351" or "IC 351" or "IC351" or
cialis? or vardenafil? or levitra?)
L50        7998 (SILDENAFIL? OR VIAGRA? OR TADALAFIL? OR "IC-351" OR "IC 351"
```

```
                OR "IC351" OR CIALIS? OR VARDENAFIL? OR LEVITRA?)
```

```
=> s (candesartan or "CV-11974" or "CV 11974" or "CV11974" or eprosartan? or
teveten? or "SKF-108566" or "SKF 108566" or "SKF108566" or irbesartan? or
"BMS-186295" or "BMS 186295" or "BMS186295" or "SR-47436" or "SR 47436" or
"SR47436" or avapro? or aprovel? or karvea?)
L51        7887 (CANDESARTAN OR "CV-11974" OR "CV 11974" OR "CV11974" OR EPROSAR
                TAN? OR TEVETEN? OR "SKF-108566" OR "SKF 108566" OR "SKF108566"
                OR IRBESARTAN? OR "BMS-186295" OR "BMS 186295" OR "BMS186295"
                OR "SR-47436" OR "SR 47436" OR "SR47436" OR AVAPRO? OR APROVEL?
                OR KARVEA?)

=> s losartan? or cozaar? or "DUP-753" or "DUP 753" or "DUP753" or "MK-954" or
"MK954" or "MK 954" or olmesartan? or olmesartan medoxomil? or "CS-866" or "CS866"
or "CS 866" or benicar? or olmetec? or votum?
L52       18908 LOSARTAN? OR COZAAR? OR "DUP-753" OR "DUP 753" OR "DUP753" OR
                "MK-954" OR "MK954" OR "MK 954" OR OLMESARTAN? OR OLMESARTAN
                MEDOXOMIL? OR "CS-866" OR "CS866" OR "CS 866" OR BENICAR? OR
                OLMETEC? OR VOTUM?

=> s saralasin? or "P-113" or "P 113" or "P113" or telmisartan? or "BIBR277" or
"BIBR-277" or "BIBR 277" or pritor? or micardis? or valsartan? or diovan? or
"CGP-48933" or "CGP 48933" or "CGP48933" or tareg? or kalpress? or miten? or nisis?
or provas? or vals?
L53       26692 SARALASIN? OR "P-113" OR "P 113" OR "P113" OR TELMISARTAN? OR
                "BIBR277" OR "BIBR-277" OR "BIBR 277" OR PRITOR? OR MICARDIS?
                OR VALSARTAN? OR DIOVAN? OR "CGP-48933" OR "CGP 48933" OR "CGP48
                933" OR TAREG? OR KALPRESS? OR MITEN? OR NISIS? OR PROVAS? OR
                VALS?

=> d his

     (FILE 'HOME' ENTERED AT 11:49:08 ON 02 MAR 2005)

     FILE 'CAPLUS' ENTERED AT 11:49:13 ON 02 MAR 2005
                E FOX DAVID/AU
L1            69 S E2-E3, E20-E22
                E HUGHES BERNADETTE/AU
L2            22 S E3-E4
                E HUGHES B/AU
L3            40 S E3
                E FOX D/AU
                E FOX D?/AU
                E FOX D/AU
L4            75 S E3
L5           144 S L1 OR L4
L6            62 S L2 OR L3
L7           204 S L5 OR L6
L8            10 S L7 AND HYPERTENSI?
L9             0 S L7 AND (CYCLIC GUANOSINE MONOPHOSPHATE (W) (PHOSPHODIESTERASE
L10            6 S L7 AND ("CGMP" OR "PDE5" OR "ANGIOTENSIN II RECEPTOR ANTAGONI

     FILE 'REGISTRY' ENTERED AT 11:57:43 ON 02 MAR 2005
                E SILDENAFIL/CN
L11            2 S E3-E4
                E TADALAFIL/CN
L12            1 S E3
                E VARDENAFIL/CN
L13            3 S E3-E5
L14            1 S CANDESARTAN/CN
                E CANDESARTAN/CN
L15            2 S E3-E5
                E EPROSARTAN/CN
L16            2 S E3-E5
```

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                E IRBESARTAN/CN
L17           4 S E3-E6
                E LOSARTAN/CN
L18           4 S E3-E7
                E OLMESARTAN/CN
L19           2 S E3-E5
                E SARALASIN/CN
L20           2 S E3-E4
                E TELMISARTAN/CN
L21           5 S E3-E7
                E VALSARTAN/CN
L22           2 S E3-E4
L23           6 S L11 OR L12 OR L13
L24          23 S L15 OR L16 OR L17 OR L18 OR L19 OR L20 OR L21 OR L22

     FILE 'CAPLUS' ENTERED AT 12:02:01 ON 02 MAR 2005
L25        1081 S L23
L26        4320 S L24
                E HYPERTENSION/BI
L27       78751 S E3, E16
                E HYPERTENSION/CT
L28       43383 S E3
L29       78751 S L27 OR L28
L30       80818 S L29 OR (HIGH BLOOD PRESSURE) OR (ELEVATED BLOOD PRESSURE) OR
L31          36 S L25 AND L26
L32           9 S L31 (L) L30
L33           9 S L30 AND L31
L34          34 S L25 (L) L30
L35        1025 S L26 (L) L30
L36           0 S L34 AND L35
L37           9 S L31 AND HYPERTENS?
L38           0 S L37 NOT L33
L39       20335 S "CGMP" OR "PDE5" OR (CYCLIC GUANOSINE MONOPHOSPHATE (W) PHOSP
L40        6539 S (ANGIOTENSIN (L) RECEPTOR ANTAGONIST) OR (ANGIOTENSIN RECEPTO
L41          80 S L39 (L) L40
L42          17 S L41 AND HYPERTENS?
L43          16 S L42 NOT L33
L44         115 S L31 OR L41
L45          15 S L44 AND (ANGINA? OR STROKE? OR DIABET? OR CONGESTIVE HEART FA
L46          11 S L45 NOT L43
L47           6 S L46 NOT L33
L48           5 S L46 NOT L47

     FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS' ENTERED AT 12:19:37 ON 02 MAR 2005
L49        7998 S (SILDENAFIL? OR VIAGRA? OR TADALAFIL? OR "IC-351" OR "IC 351"
L50        7998 S (SILDENAFIL? OR VIAGRA? OR TADALAFIL? OR "IC-351" OR "IC 351"
L51        7887 S (CANDESARTAN OR "CV-11974" OR "CV 11974" OR "CV11974" OR EPRO
L52       18908 S LOSARTAN? OR COZAAR? OR "DUP-753" OR "DUP 753" OR "DUP753" OR
L53       26692 S SARALASIN? OR "P-113" OR "P 113" OR "P113" OR TELMISARTAN? OR

=> d cost
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                 ENTRY    SESSION
CONNECT CHARGES                                  12.62      32.13
NETWORK CHARGES                                   0.48       3.54
SEARCH CHARGES                                    0.00     266.02
DISPLAY CHARGES                                   0.00     137.80
                                                -------    -------
FULL ESTIMATED COST                              13.10     439.49

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)    SINCE FILE      TOTAL
                                                 ENTRY    SESSION
CA SUBSCRIBER PRICE                               0.00     -37.96
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IN FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS' AT 12:24:58 ON 02 MAR 2005

```
=> s l51 or l52 or l53
L54       48656 L51 OR L52 OR L53

=> s l50 and l54
L55         130 L50 AND L54

=> s l55 (L) (hypertens? or (high blood pressure? or elevated blood pressure? or
(increase? blood pressure)))
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L79 (L) '
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L80 (L) '
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L81 (L) '
   3 FILES SEARCHED...
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L82 (L) '
L56          46 L55 (L) (HYPERTENS? OR (HIGH BLOOD PRESSURE? OR ELEVATED BLOOD
                PRESSURE? OR (INCREASE? BLOOD PRESSURE)))

=> dup rem l56
PROCESSING COMPLETED FOR L56
L57           45 DUP REM L56 (1 DUPLICATE REMOVED)
                 ANSWER '1' FROM FILE MEDLINE
                 ANSWER '2' FROM FILE BIOSIS
                 ANSWERS '3-34' FROM FILE EMBASE
                 ANSWERS '35-45' FROM FILE WPIDS

=> d 157 1-45
THE ESTIMATED COST FOR THIS REQUEST IS 133.77 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N:n
REQUEST CANCELED

=> s l55 and hypertens?
L58          46 L55 AND HYPERTENS?

=> d cost
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
CONNECT CHARGES                                        22.87      42.38
NETWORK CHARGES                                         0.78       3.84
SEARCH CHARGES                                          0.00     266.02
DISPLAY CHARGES                                         0.00     137.80
                                                    -------    -------
FULL ESTIMATED COST                                    23.65     450.04

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                       ENTRY    SESSION
CA SUBSCRIBER PRICE                                     0.00     -37.96

IN FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS' AT 12:27:36 ON 02 MAR 2005


=> d 157 scan

L57  45  ANSWERS  WPIDS  COPYRIGHT 2005 THE THOMSON CORP on STN

AN   2003-720097 [68]   WPIDS
TI   Propellant free buccal spray composition used for increasing rapid
     absorption of active compounds, comprises active compound such as
     antiarrhythmic, antihypertensive, heart regulator or vasodilator and polar
```

solvent.

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):.

L57 45 ANSWERS WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN

AN 2001-475649 [51] WPIDS
TI Solid composition for delivery of active agents e.g. glyburide comprises carrier optionally containing a substrate having an encapsulation coat containing hydrophilic surfactants e.g. polyoxyethylene alkylethers.

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):.

L57 45 ANSWERS WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN

AN 2000-147185 [13] WPIDS
TI Nitrate salts of antihypertensive agents.

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):.

L57 45 ANSWERS BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
TI Different effect of **valsartan** and lisinopril on **sildenafil** use in **hypertensive** men with erectile dysfunction.
IT Miscellaneous Descriptors
drug dosage; drug efficacy; Meeting Abstract

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):.

L57 45 ANSWERS WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN

AN 2004-525396 [50] WPIDS
TI New cyclopentyl substituted glutaramide derivatives are neutral endopeptidase inhibitors useful for the treatment or prevention of e.g. cardiovascular disease, **hypertension** and sexual dysfunction.

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):.

L57 45 ANSWERS WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN

AN 2004-525387 [50] WPIDS
TI New cyclopentyl substituted glutaramide derivatives useful as neutral endopeptidase selective inhibitors for treating or preventing conditions such as **hypertension**, female sexual dysfunction and male erectile dysfunction.

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):.

L57 45 ANSWERS WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN

AN 2004-091044 [09] WPIDS
TI Combination useful for treating **hypertension**, congestive heart failure and diabetes comprises a cyclic guanosine monophosphate specific phosphodiesterase type 5 inhibitor and an angiotensin II receptor antagonist.

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):.

L57 45 ANSWERS WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN

AN 2004-675638 [66] WPIDS
TI New 3-(1-(3-(1,3-benzothiazol-6-yl) propylcarbamoyl)cycloalkyl) propianic acid derivatives are neutral endopeptidase enzyme inhibitors useful for the treatment of e.g. stroke, glaucoma, obesity, metabolic disease and

epilepsy.

```
HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):end

=> d his

     (FILE 'HOME' ENTERED AT 11:49:08 ON 02 MAR 2005)

     FILE 'CAPLUS' ENTERED AT 11:49:13 ON 02 MAR 2005
                E FOX DAVID/AU
L1           69 S E2-E3, E20-E22
                E HUGHES BERNADETTE/AU
L2           22 S E3-E4
                E HUGHES B/AU
L3           40 S E3
                E FOX D/AU
                E FOX D?/AU
                E FOX D/AU
L4           75 S E3
L5          144 S L1 OR L4
L6           62 S L2 OR L3
L7          204 S L5 OR L6
L8           10 S L7 AND HYPERTENSI?
L9            0 S L7 AND (CYCLIC GUANOSINE MONOPHOSPHATE (W) (PHOSPHODIESTERASE
L10           6 S L7 AND ("CGMP" OR "PDE5" OR "ANGIOTENSIN II RECEPTOR ANTAGONI

     FILE 'REGISTRY' ENTERED AT 11:57:43 ON 02 MAR 2005
                E SILDENAFIL/CN
L11           2 S E3-E4
                E TADALAFIL/CN
L12           1 S E3
                E VARDENAFIL/CN
L13           3 S E3-E5
L14           1 S CANDESARTAN/CN
                E CANDESARTAN/CN
L15           2 S E3-E5
                E EPROSARTAN/CN
L16           2 S E3-E5
                E IRBESARTAN/CN
L17           4 S E3-E6
                E LOSARTAN/CN
L18           4 S E3-E7
                E OLMESARTAN/CN
L19           2 S E3-E5
                E SARALASIN/CN
L20           2 S E3-E4
                E TELMISARTAN/CN
L21           5 S E3-E7
                E VALSARTAN/CN
L22           2 S E3-E4
L23           6 S L11 OR L12 OR L13
L24          23 S L15 OR L16 OR L17 OR L18 OR L19 OR L20 OR L21 OR L22

     FILE 'CAPLUS' ENTERED AT 12:02:01 ON 02 MAR 2005
L25        1081 S L23
L26        4320 S L24
                E HYPERTENSION/BI
L27       78751 S E3, E16
                E HYPERTENSION/CT
L28       43383 S E3
L29       78751 S L27 OR L28
L30       80818 S L29 OR (HIGH BLOOD PRESSURE) OR (ELEVATED BLOOD PRESSURE) OR
L31          36 S L25 AND L26
L32           9 S L31 (L) L30
```

```
L33           9 S L30 AND L31
L34          34 S L25 (L) L30
L35        1025 S L26 (L) L30
L36           0 S L34 AND L35
L37           9 S L31 AND HYPERTENS?
L38           0 S L37 NOT L33
L39       20335 S "CGMP" OR "PDE5" OR (CYCLIC GUANOSINE MONOPHOSPHATE (W) PHOSP
L40        6539 S (ANGIOTENSIN (L) RECEPTOR ANTAGONIST) OR (ANGIOTENSIN RECEPTO
L41          80 S L39 (L) L40
L42          17 S L41 AND HYPERTENS?
L43          16 S L42 NOT L33
L44         115 S L31 OR L41
L45          15 S L44 AND (ANGINA? OR STROKE? OR DIABET? OR CONGESTIVE HEART FA
L46          11 S L45 NOT L43
L47           6 S L46 NOT L33
L48           5 S L46 NOT L47

     FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS' ENTERED AT 12:19:37 ON 02 MAR 2005
L49        7998 S (SILDENAFIL? OR VIAGRA? OR TADALAFIL? OR "IC-351" OR "IC 351"
L50        7998 S (SILDENAFIL? OR VIAGRA? OR TADALAFIL? OR "IC-351" OR "IC 351"
L51        7887 S (CANDESARTAN OR "CV-11974" OR "CV 11974" OR "CV11974" OR EPRO
L52       18908 S LOSARTAN? OR COZAAR? OR "DUP-753" OR "DUP 753" OR "DUP753" OR
L53       26692 S SARALASIN? OR "P-113" OR "P 113" OR "P113" OR TELMISARTAN? OR
L54       48656 S L51 OR L52 OR L53
L55         130 S L50 AND L54
L56          46 S L55 (L) (HYPERTENS? OR (HIGH BLOOD PRESSURE? OR ELEVATED BLOO
L57          45 DUP REM L56 (1 DUPLICATE REMOVED)
L58          46 S L55 AND HYPERTENS?

=> s (155 and hypertens?)/ab
QUALIFICATION NOT VALID FOR L55
Field code qualifications can only be applied to text
terms.

=> d l57 1-45 trial
NO VALID FORMATS ENTERED FOR FILE 'BIOSIS'
In a multifile environment, each file must have at least one valid
format requested.  Refer to file specific help messages or the
STNGUIDE file for information on formats available in individual
files.
REENTER DISPLAY FORMAT FOR ALL FILES (FILEDEFAULT):title
'TITLE' IS NOT A VALID FORMAT
In a multifile environment, a format can only be used if it is valid
in at least one of the files.  Refer to file specific help messages
or the STNGUIDE file for information on formats available in
individual files.
REENTER DISPLAY FORMAT FOR ALL FILES (FILEDEFAULT):ti

L57  ANSWER 1 OF 45     MEDLINE on STN                  DUPLICATE 1
TI   Interactions between grapefruit juice and cardiovascular drugs.

L57  ANSWER 2 OF 45  BIOSIS  COPYRIGHT (c) 2005 The Thomson Corporation  on STN
TI   Different effect of valsartan and lisinopril on
     sildenafil use in hypertensive men with erectile
     dysfunction.

L57  ANSWER 3 OF 45  EMBASE  COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
     on STN
TI   New drugs approved by the FDA; New dosage forms and indications; Agents
     pending FDA approval; Significant labeling changes related to safety.

L57  ANSWER 4 OF 45  EMBASE  COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
     on STN
TI   Highlights of the year in JACC 2004.
```

L57 ANSWER 5 OF 45 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
TI Drug-induced atrial fibrillation.

L57 ANSWER 6 OF 45 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
TI Gateways to clinical trials: December 2004.

L57 ANSWER 7 OF 45 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
TI Pilot assessment of the response of several pulmonary hemodynamic variables to sublingual **sildenafil** in candidates for heart transplantation.

L57 ANSWER 8 OF 45 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
TI ACC/AHA guidelines for the management of patients with ST-elevation myocardial infarction - Executive summary: A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (writing committee to revise the 1999 guidelines for the management of patients with acute myocardial infarction).

L57 ANSWER 9 OF 45 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
TI Gateways to Clinical Trials: July/August 2004.

L57 ANSWER 10 OF 45 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
TI Stand by your brand.

L57 ANSWER 11 OF 45 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
TI [New advances in drug therapy in 2003-2004].
ACTUALITES THERAPEUTIQUES 2003-2004 (1).

L57 ANSWER 12 OF 45 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
TI Scleroderma - Clinical and pathological advances.

L57 ANSWER 13 OF 45 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
TI Erectile dysfunction: A need for greater awareness.

L57 ANSWER 14 OF 45 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
TI Diastolic dysfunction.

L57 ANSWER 15 OF 45 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
TI The Year's New Drugs.

L57 ANSWER 16 OF 45 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
TI The top 12 advances in vascular medicine.

L57 ANSWER 17 OF 45 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
TI Pharmacy prepares for the leap year.

L57 ANSWER 18 OF 45 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
TI Interactions of grapefruit juice and cardiovascular medications: A potential risk of toxicity.

L57 ANSWER 19 OF 45 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
TI Active drug metabolites in drug development.

L57 ANSWER 20 OF 45 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
TI New drug approvals for 2002.

L57 ANSWER 21 OF 45 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
TI Sexual dysfunction in men and women with chronic kidney disease and end-stage kidney disease.

L57 ANSWER 22 OF 45 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
TI New drugs with novel therapeutic characteristics. Have they been subject to randomized controlled trials?.

L57 ANSWER 23 OF 45 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
TI Management of systemic sclerosis.

L57 ANSWER 24 OF 45 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
TI [New advances in drug therapy in the year 2002].
ACTUALITES THERAPEUTIQUES 2002.

L57 ANSWER 25 OF 45 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
TI Pulmonary **hypertension**: Current criteria for diagnosis and treatment.

L57 ANSWER 26 OF 45 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
TI Erectile dysfunction and **hypertension**.

L57 ANSWER 27 OF 45 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
TI Opinion and evidence in cardiovascular therapeutics.

L57 ANSWER 28 OF 45 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
TI The choice of antihypertensive drugs in patients with erectile dysfunction.

L57 ANSWER 29 OF 45 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
TI The effect of a **losartan**-based treatment regimen on isolated systolic **hypertension**.

L57 ANSWER 30 OF 45 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
TI BMS takes Vanlev to the FDA.

L57 ANSWER 31 OF 45 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
TI Lercanidipine: A novel dihydropyridine calcium-channel blocker.

L57 ANSWER 32 OF 45 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
TI [Treatment of erectile dysfunction with **sildenafil** in patients with miocardic revascularization].
TRATAMENTO DA DISFUNCAO ERETIL COM **SILDENAFIL** EM PACIENTES COM

REVASCULARIZACAO MIOCARDICA.

L57 ANSWER 33 OF 45 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
TI **Sildenafil** (**viagra**ρ): Use and precautions in patients with cardiovascular disease.

L57 ANSWER 34 OF 45 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
TI New molecular entities approved in 1998.

L57 ANSWER 35 OF 45 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
TI New cyclopentyl substituted glutaramide derivatives are neutral endopeptidase inhibitors useful for the treatment or prevention of e.g. cardiovascular disease, **hypertension** and sexual dysfunction.

L57 ANSWER 36 OF 45 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
TI New cyclopentyl substituted glutaramide derivatives useful as neutral endopeptidase selective inhibitors for treating or preventing conditions such as **hypertension**, female sexual dysfunction and male erectile dysfunction.

L57 ANSWER 37 OF 45 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
TI Combination useful for treating **hypertension**, congestive heart failure and diabetes comprises a cyclic guanosine monophosphate specific phosphodiesterase type 5 inhibitor and an angiotensin II receptor antagonist.

L57 ANSWER 38 OF 45 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
TI New 3-(1-(3-(1,3-benzothiazol-6-yl) propylcarbamoyl)cycloalkyl) propianic acid derivatives are neutral endopeptidase enzyme inhibitors useful for the treatment of e.g. stroke, glaucoma, obesity, metabolic disease and epilepsy.

L57 ANSWER 39 OF 45 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
TI Nifedipine composition used for treating angina pectoris and **hypertension**, includes particles of nifedipine or its salt, and surface stabilizer.

L57 ANSWER 40 OF 45 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
TI Treatment of vascular condition e.g. sexual dysfunction, atherosclerosis involves administrating a combination of at least two agents selected from anti-pressor agent, endothelin antagonist and sex hormone.

L57 ANSWER 41 OF 45 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
TI New polycyclic guanine derivatives useful for treating urological, vascular and pulmonary disorders.

L57 ANSWER 42 OF 45 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
TI Production of cationic non-viral delivery vehicle useful e.g. for DNA lipofection or targeted drug delivery, by conjugating steroid or other drug with polyamine and mixing with lipid.

L57 ANSWER 43 OF 45 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
TI Propellant free buccal spray composition used for increasing rapid absorption of active compounds, comprises active compound such as antiarrhythmic, antihypertensive, heart regulator or vasodilator and polar solvent.

L57 ANSWER 44 OF 45 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
TI Solid composition for delivery of active agents e.g. glyburide comprises carrier optionally containing a substrate having an encapsulation coat containing hydrophilic surfactants e.g. polyoxyethylene alkylethers.

L57 ANSWER 45 OF 45 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
TI Nitrate salts of antihypertensive agents.

=> d l57 2,4,16,22,25,26,28,29,37,39,40 ibib ed abs

L57 ANSWER 2 OF 45 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 2002:355141 BIOSIS
DOCUMENT NUMBER: PREV200200355141
TITLE: Different effect of **valsartan** and lisinopril on **sildenafil** use in **hypertensive** men with erectile dysfunction.
AUTHOR(S): Fogari, Roberto [Reprint author]; Preti, Paola [Reprint author]; Mugellini, Amedeo [Reprint author]; Derosa, Giuseppe [Reprint author]; Marasi, Gianluigi [Reprint author]; Corradi, Luca [Reprint author]; Zoppi, Annalisa [Reprint author]; Poletti, Luigi [Reprint author]; Rinaldi, Andrea [Reprint author]
CORPORATE SOURCE: Department of Internal Medicine and Therapeutics, University of Pavia-IRCCS Policlinico S. Matteo, Pavia, Italy
SOURCE: American Journal of Hypertension, (April, 2002) Vol. 15, No. 4 Part 2, pp. 37A. print.
Meeting Info.: Seventeenth Annual Scientific Meeting of the American Society of Hypertension. New York, N.Y., USA. May 14-18, 2002.
CODEN: AJHYE6. ISSN: 0895-7061.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 26 Jun 2002
Last Updated on STN: 26 Jun 2002
ED Entered STN: 26 Jun 2002
Last Updated on STN: 26 Jun 2002

L57 ANSWER 4 OF 45 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2005015181 EMBASE
TITLE: Highlights of the year in JACC 2004.
AUTHOR: Demaria A.N.; Ben-Yehuda O.; Berman D.; Feld G.K.; Greenberg B.H.; Knoke J.D.; Knowlton K.U.; Lew W.Y.W.; Narula J.; Sahn D.; Tsimikas S.
CORPORATE SOURCE: . ademaria@usd.edu
SOURCE: Journal of the American College of Cardiology, (4 Jan 2005) 45/1 (137-153).
Refs: 108
ISSN: 0735-1097 CODEN: JACCDI
PUBLISHER IDENT.: S 0735-1097(04)02233-8
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
027 Biophysics, Bioengineering and Medical Instrumentation
036 Health Policy, Economics and Management
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English

L57 ANSWER 16 OF 45 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2005034923 EMBASE
TITLE: The top 12 advances in vascular medicine.
AUTHOR: Olin J.W.; Jang J.; Jaff M.R.; Beckman J.A.; Rooke T.
CORPORATE SOURCE: Dr. J.W. Olin, Department of Medicine, Mount Sinai School

of Medicine, Box 1033, One Gustave L. Levy Place, New York, NY 10029, United States. jeffrey.olin@msnyuhealth.org

SOURCE: Journal of Endovascular Therapy, (2004) 11/SUPPL. 2 (II21-II31).
Refs: 82
ISSN: 1526-6028 CODEN: JENTFI

COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 017 Public Health, Social Medicine and Epidemiology
018 Cardiovascular Diseases and Cardiovascular Surgery
036 Health Policy, Economics and Management
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English

AB In the past decade, impressive strides have been made in the diagnosis and management of atherosclerotic, aneurysmal, and thromboembolic diseases, thanks in large part to the explosive growth in both vascular biology and clinical vascular medicine. We review what we consider to be the top 12 advances in this field: the discovery of nitric oxide, the metabolic syndrome, new thrombophilic disorders, therapeutic angiogenesis, endoluminal treatment of chronic venous disease, and a variety of drugs, including **sildenafil**, cilostazol, low-molecular-weight heparins, oral direct thrombin inhibitors, clopidogrel, statins, and angiotensin-converting enzyme inhibitors and angiotensin-receptor blocking agents.

L57 ANSWER 22 OF 45 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2002375393 EMBASE
TITLE: New drugs with novel therapeutic characteristics. Have they been subject to randomized controlled trials?.
AUTHOR: Lexchin J.
CORPORATE SOURCE: Dr. J. Lexchin, 121 Walmer Rd., Toronto, Ont. M5R 2X8, Canada. joel.lexchin@utoronto.ca
SOURCE: Canadian Family Physician, (1 Sep 2002) 48/SEPT. (1487-1492).
Refs: 8
ISSN: 0008-350X CODEN: CFPHAJ

COUNTRY: Canada
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 017 Public Health, Social Medicine and Epidemiology
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English; French

AB Objective. To determine how many randomized controlled trials on the safety or efficacy of new drugs are published when these drugs are first marketed in Canada, and to determine the quality of the information in those trials. Design. A MEDLINE search was conducted on each drug identified as having novel therapeutic characteristics and first marketed between 1990 and 2000. Main Outcome Measures. Number of trials dealing with the safety or efficacy of each drug published at the time the drug was marketed. Number of patients taking the study drug, length of the trial, and type of control. Results. The number of trials varied substantially. For some drugs, there were more than 20 studies; for others only a single study. Many trials were small and short-term, and used placebo controls. Conclusion. Too few trials or inadequate trials on the safety and efficacy of new drugs are published when these drugs are first marketed in Canada. The lack of published trials means that physicians do not know whether results are generalizable to their patients, how to position the drug in relation to other treatments, or whether the drugs have long-term safety and efficacy.

L57 ANSWER 25 OF 45 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2002192173 EMBASE
TITLE: Pulmonary **hypertension**: Current criteria for diagnosis and treatment.
AUTHOR: Barbera J.A.
CORPORATE SOURCE: Dr. J.A. Barbera, Servei de Pneumologia, Hospital Clinic, Universidad de Barcelona, Villarroel 170, 08036 Barcelona, Spain. jbarbera@clinic.ub.es
SOURCE: Medicina Clinica, (27 Apr 2002) 118/15 (590-596).
Refs: 41
ISSN: 0025-7753 CODEN: MCLBA2
COUNTRY: Spain
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 006 Internal Medicine
015 Chest Diseases, Thoracic Surgery and Tuberculosis
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English

L57 ANSWER 26 OF 45 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2002334549 EMBASE
TITLE: Erectile dysfunction and **hypertension**.
AUTHOR: Jackson G.
SOURCE: International Journal of Clinical Practice, (2002) 56/7 (491-493).
Refs: 15
ISSN: 1368-5031 CODEN: IJCPF
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Editorial
FILE SEGMENT: 006 Internal Medicine
018 Cardiovascular Diseases and Cardiovascular Surgery
028 Urology and Nephrology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English

L57 ANSWER 28 OF 45 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2002165920 EMBASE
TITLE: The choice of antihypertensive drugs in patients with erectile dysfunction.
AUTHOR: Khan M.A.; Morgan R.J.; Mikhailidis D.P.
CORPORATE SOURCE: Dr. D.P. Mikhailidis, Department of Clinical Biochemistry, Roy. Free/Univ. Coll. Med. School, Royal Free Campus, Pond Street, London NW3 2QG, United Kingdom. mikhailidis@hotmail.com
SOURCE: Current Medical Research and Opinion, (2002) 18/2 (103-107).
Refs: 35
ISSN: 0300-7995 CODEN: CMROCX
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; (Short Survey)
FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
028 Urology and Nephrology
036 Health Policy, Economics and Management
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
AB It is well established that **hypertension** and the more traditional anti-**hypertensive** drugs are associated with erectile dysfunction (ED). There is evidence showing that two antihypertensive

drugs - doxazosin and **losartan** - have a positive effect on erectile function. Therefore these drugs may decrease the incidence of ED in patients who need treatment for **hypertension**. Doxazosin and/or **losartan** can also be beneficial in patients who develop ED after starting treatment with other antihypertensive drugs. These options could, in turn, ensure better compliance and blood pressure control. A fall in the overall cost of treatment will also be anticipated if there is a reduced need for drugs prescribed for ED in patients with **hypertension**.

L57 ANSWER 29 OF 45 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2002139468 EMBASE
TITLE: The effect of a **losartan**-based treatment regimen on isolated systolic **hypertension**.
AUTHOR: Cushman W.C.; Brady W.E.; Gazdick L.P.; Zeldin R.K.
CORPORATE SOURCE: Dr. W.C. Cushman, Veterans Affairs Medical Center, Preventive Medicine Section 111Q, 1030 Jefferson Avenue, Memphis, TN 38104, United States
SOURCE: Journal of Clinical Hypertension, (2002) 4/2 (101-107). Refs: 23
ISSN: 1524-6175 CODEN: JCHYFN
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 006 Internal Medicine
018 Cardiovascular Diseases and Cardiovascular Surgery
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English

AB This study was conducted to compare the antihypertensive efficacy and tolerability, over 12 weeks, of a **losartan**-based treatment regimen and placebo in patients with isolated systolic **hypertension**. Three hundred eight patients ≥35 years of age with isolated systolic **hypertension**, defined as trough sitting blood pressure between 140 and 200 mm Hg systolic and between 70 and 89 mm Hg diastolic, were randomized to **losartan** 50 mg (n=157) or placebo (n=151) once daily, with titration as necessary to achieve a goal trough sitting systolic blood pressure (SBP) <140 mm Hg. At baseline, mean trough sitting SBP was 140-159 mm Hg in 20.5% of patients, 160-179 mm Hg in 62.7%, and 180-200 mm Hg in 16.9%, and was similar in the two groups (**losartan**, 165.3 mm Hg; placebo, 166.1 mm Hg). At 12 weeks, mean trough sitting SBP decreased significantly ($p<0.001$) in both the **losartan**-based treatment group (by 19.2 mm Hg) and in the placebo group (by 7.6 mm Hg). The reduction in sitting SBP was significantly greater for **losartan** than placebo (-11.6 mm Hg; 95% confidence interval, -14.8 to -8.4). In patients with isolated systolic **hypertension**, a once-daily **losartan**-based treatment regimen significantly lowered SBP. The **losartan**-based regimen exhibited antihypertensive efficacy that was superior to that of placebo, with a similar tolerability profile.

L57 ANSWER 37 OF 45 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN

ACCESSION NUMBER: 2004-091044 [09] WPIDS
DOC. NO. CPI: C2004-037098
TITLE: Combination useful for treating **hypertension**, congestive heart failure and diabetes comprises a cyclic guanosine monophosphate specific phosphodiesterase type 5 inhibitor and an angiotensin II receptor antagonist.
DERWENT CLASS: B02
INVENTOR(S): FOX, D N A; HUGHES, B
PATENT ASSIGNEE(S): (FOXD-I) FOX D N A; (HUGH-I) HUGHES B; (PFIZ) PFIZER INC; (PFIZ) PFIZER LTD

COUNTRY COUNT: 103
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2004002461	A2	20040108	(200409)*	EN	25
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PH PL PT RO RU SC SD SE SG SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW					
US 2004132731	A1	20040708	(200445)		
AU 2003242895	A1	20040119	(200447)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2004002461	A2	WO 2003-IB2657	20030616
US 2004132731	A1 Provisional	US 2002-396780P	20020717
		US 2003-603369	20030625
AU 2003242895	A1	AU 2003-242895	20030616

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2003242895	A1 Based on	WO 2004002461

PRIORITY APPLN. INFO: GB 2002-14784 20020626
ED 20040205
AN 2004-091044 [09] WPIDS
AB WO2004002461 A UPAB: 20040205
NOVELTY - Combination (I) of an inhibitor of cyclic guanosine monophosphate specific phosphodiesterase type 5 (PDE5) (A) and an angiotensin II receptor antagonist (B) for the preparation of a medicament for the palliative, curative or prophylactic treatment of **hypertension**, congestive heart failure, angina, stroke, diabetes and impaired glucose tolerance, is new.

DETAILED DESCRIPTION - Combination (I) of an inhibitor of cyclic guanosine monophosphate specific phosphodiesterase type 5 (PDE5) (A) and an angiotensin II receptor antagonist (B) for the preparation of a medicament for the palliative, curative or prophylactic treatment of **hypertension**, including essential **hypertension**, pulmonary **hypertension**, secondary **hypertension**, isolated systolic **hypertension**, **hypertension** associated with diabetes, **hypertension** associated with atherosclerosis and renovascular **hypertension**, congestive heart failure, angina, stroke, diabetes and impaired glucose tolerance, is new.

INDEPENDENT CLAIMS are also included for the following:

(1) A composition comprising (A) and (B); and

(2) A kit for treating **hypertension** comprising a first composition comprising (A) and a second composition comprising (B) and a container for the compositions.

ACTIVITY - Hypotensive; Respiratory-Gen.; Antidiabetic; Cardiovasular-Gen.; Antianginal; Cerebroprotective; Vasotropic.

MECHANISM OF ACTION - Cyclic guanosine monophosphate specific phosphodiesterase type 5 (PDE5) inhibitor; Angiotensin II receptor antagonist.

USE - (I) is useful for the palliative, curative or prophylactic treatment of **hypertension** (including essential **hypertension**, pulmonary **hypertension**, secondary

hypertension, isolated systolic **hypertension**, **hypertension** associated with diabetes, **hypertension** associated with atherosclerosis and renovascular **hypertension**), congestive heart failure, angina, stroke, diabetes and impaired glucose tolerance (claimed).

(I) was tested for its efficacy in rats. The results showed that (I) was effective for the fall of mean arterial pressure (MAP) to 32.6 mmHg which was significantly larger than the sum of the two individual effects (7.4 mmHg for PDE5 inhibitor and 3.2 mmHg for **candesartan**) (p=0.058).

ADVANTAGE - (I) is more potent and less toxic.

Dwg.0/0

L57 ANSWER 39 OF 45 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN

ACCESSION NUMBER: 2004-478988 [45] WPIDS

CROSS REFERENCE: 2000-303363 [26]; 2001-281805 [29]; 2002-425895 [45]; 2003-183864 [18]; 2003-708770 [67]; 2003-767190 [72]; 2003-897031 [82]; 2004-190670 [18]; 2004-191100 [18]; 2004-327673 [30]; 2004-579872 [56]; 2004-603323 [58]; 2005-121249 [13]

DOC. NO. NON-CPI: N2004-377675

DOC. NO. CPI: C2004-178302

TITLE: Nifedipine composition used for treating angina pectoris and **hypertension**, includes particles of nifedipine or its salt, and surface stabilizer.

DERWENT CLASS: A96 B03 P34

INVENTOR(S): MERISKO-LIVERSIDGE, E

PATENT ASSIGNEE(S): (ELAN-N) ELAN PHARMA INT LTD

COUNTRY COUNT: 1

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 2004115134	A1	20040617	(200445)*		28

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
US 2004115134	A1	CIP of	US 1999-337675	19990622
		Cont of	US 2000-666539	20000921
		Cont of	US 2000-715117	20001120
		CIP of	WO 2001-US15983	20010518
		CIP of	US 2002-75443	20020215
		CIP of	US 2003-276400	20030115
		CIP of	US 2003-345312	20030116
			US 2003-712259	20031114

FILING DETAILS:

PATENT NO	KIND		PATENT NO
US 2004115134	A1	Cont of	US 6375986
		CIP of	US 6592903

PRIORITY APPLN. INFO: US 2003-712259 20031114; US 1999-337675 19990622; US 2000-666539 20000921; US 2000-715117 20001120; WO 2001-US15983 20010518; US 2002-75443 20020215; US 2003-276400 20030115; US 2003-345312 20030116

ED 20040716

AN 2004-478988 [45] WPIDS
CR 2000-303363 [26]; 2001-281805 [29]; 2002-425895 [45]; 2003-183864 [18]; 2003-708770 [67]; 2003-767190 [72]; 2003-897031 [82]; 2004-190670 [18]; 2004-191100 [18]; 2004-327673 [30]; 2004-579872 [56]; 2004-603323 [58]; 2005-121249 [13]

AB US2004115134 A UPAB: 20050224

NOVELTY - A nifedipine composition comprises particles of nifedipine or its salt, where the nifedipine particles have an effective average particle size of less than 2000 nm; and a surface stabilizer.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a method of making a nifedipine composition comprising contacting particles of nifedipine or its salt with a surface stabilizer(s), providing a composition having an average particle size of less than 200 nm.

ACTIVITY - Antianginal; Hypotensive; Vasotropic.

MECHANISM OF ACTION - Calcium channel blocker.

USE - The invention is used as a vasodilating agent and a hypotensive medicament for the remedy of angina pectoris and **hypertension**.

ADVANTAGE - The invention can be readily absorbed by a human, or other animal, decreases frequency of dosing, improves clinical efficacy, and potentially reduces side effects.

DESCRIPTION OF DRAWING(S) - The figure shows the mean in vivo plasma profiles of nifedipine after single dosed, fasted, administration in humans.

Dwg.1/2

L57 ANSWER 40 OF 45 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 2004-294421 [27] WPIDS
CROSS REFERENCE: 2000-237773 [20]
DOC. NO. CPI: C2004-112620
TITLE: Treatment of vascular condition e.g. sexual dysfunction, atherosclerosis involves administrating a combination of at least two agents selected from anti-pressor agent, endothelin antagonist and sex hormone.
DERWENT CLASS: B05
INVENTOR(S): ADAMS, M A; HALE, T M; HEATON, J P W
PATENT ASSIGNEE(S): (CALL-N) CALLEGY PHARM INC; (TOOH) UNIV QUEENS KINGSTON
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 2004063719	A1	20040401	(200427)*		29

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
US 2004063719	A1	Provisional	US 1998-98178P	19980826
		Cont of	US 1999-382749	19990825
		Cont of	US 2001-902787	20010712
		Provisional	US 2002-377917P	20020502
		CIP of	US 2002-192281	20020709
			US 2003-429197	20030502

FILING DETAILS:

PATENT NO	KIND		PATENT NO
US 2004063719	A1	Cont of	US 6284763
		Cont of	US 6458797

PRIORITY APPLN. INFO: US 2003-429197 20030502; US
1998-98178P 19980826; US
1999-382749 19990825; US

	2001-902787	20010712; US
	2002-377917P	20020502; US
	2002-192281	20020709

ED 20040426
AN 2004-294421 [27] WPIDS
CR 2000-237773 [20]
AB US2004063719 A UPAB: 20040426
NOVELTY - Treatment of vascular condition involves administration of a combination of at least two agents selected from an anti-pressor agent, an endothelin antagonist and a sex hormone.

ACTIVITY - Vasotropic; Uropathic; Gynecological; Antiinflammatory; Antidiabetic; Antiarteriosclerotic; Nephrotropic; Hypotensive; Ophthalmological; Neuroprotective; Cardiant.

MECHANISM OF ACTION - None given.

USE - For treatment of vascular conditions such as male sexual dysfunction (e.g. erectile dysfunction, priapism and premature ejaculation), female sexual dysfunction (e.g. vaginal lubrication, vaginal engorgement, pain during intercourse, dyspareunia, urogenital infection, post-menopause, diabetes, vascular disease, estrogen depletion condition, idiosyncratic vaginal dryness, vaginismus, vulvodynia, interstitial cystitis, nonspecific urethritis, sexual arousal disorder, hypoactive desire disorder and sexual orgasmic disorder), atherosclerosis, renal failure, **hypertension**, congestive heart failure, diabetic retinopathy and diabetic neuropathy (all claimed).

ADVANTAGE - The endothelin antagonist eliminates or reduces anti-pressor tolerance. The combination therapy enhances the efficacy of the anti-pressor agent and enables increase in the frequency and duration of anti-pressor administration for long-term treatment of vascular conditions.

Dwg.0/10

```
=> d cost
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
CONNECT CHARGES                                        46.99      66.50
NETWORK CHARGES                                         1.38       4.44
SEARCH CHARGES                                          0.00     266.02
DISPLAY CHARGES                                        32.75     170.55
                                                      -------    -------
FULL ESTIMATED COST                                    81.12     507.51

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                       ENTRY    SESSION
CA SUBSCRIBER PRICE                                     0.00     -37.96

IN FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS' AT 12:33:55 ON 02 MAR 2005


=> save
ENTER L#, L# RANGE, ALL, OR (END):end

=> d his

     (FILE 'HOME' ENTERED AT 11:49:08 ON 02 MAR 2005)

     FILE 'CAPLUS' ENTERED AT 11:49:13 ON 02 MAR 2005
                E FOX DAVID/AU
L1           69 S E2-E3, E20-E22
                E HUGHES BERNADETTE/AU
L2           22 S E3-E4
                E HUGHES B/AU
L3           40 S E3
                E FOX D/AU
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                E FOX D?/AU
                E FOX D/AU
L4           75 S E3
L5          144 S L1 OR L4
L6           62 S L2 OR L3
L7          204 S L5 OR L6
L8           10 S L7 AND HYPERTENSI?
L9            0 S L7 AND (CYCLIC GUANOSINE MONOPHOSPHATE (W) (PHOSPHODIESTERASE
L10           6 S L7 AND ("CGMP" OR "PDE5" OR "ANGIOTENSIN II RECEPTOR ANTAGONI

     FILE 'REGISTRY' ENTERED AT 11:57:43 ON 02 MAR 2005
                E SILDENAFIL/CN
L11           2 S E3-E4
                E TADALAFIL/CN
L12           1 S E3
                E VARDENAFIL/CN
L13           3 S E3-E5
L14           1 S CANDESARTAN/CN
                E CANDESARTAN/CN
L15           2 S E3-E5
                E EPROSARTAN/CN
L16           2 S E3-E5
                E IRBESARTAN/CN
L17           4 S E3-E6
                E LOSARTAN/CN
L18           4 S E3-E7
                E OLMESARTAN/CN
L19           2 S E3-E5
                E SARALASIN/CN
L20           2 S E3-E4
                E TELMISARTAN/CN
L21           5 S E3-E7
                E VALSARTAN/CN
L22           2 S E3-E4
L23           6 S L11 OR L12 OR L13
L24          23 S L15 OR L16 OR L17 OR L18 OR L19 OR L20 OR L21 OR L22

     FILE 'CAPLUS' ENTERED AT 12:02:01 ON 02 MAR 2005
L25        1081 S L23
L26        4320 S L24
                E HYPERTENSION/BI
L27       78751 S E3, E16
                E HYPERTENSION/CT
L28       43383 S E3
L29       78751 S L27 OR L28
L30       80818 S L29 OR (HIGH BLOOD PRESSURE) OR (ELEVATED BLOOD PRESSURE) OR
L31          36 S L25 AND L26
L32           9 S L31 (L) L30
L33           9 S L30 AND L31
L34          34 S L25 (L) L30
L35        1025 S L26 (L) L30
L36           0 S L34 AND L35
L37           9 S L31 AND HYPERTENS?
L38           0 S L37 NOT L33
L39       20335 S "CGMP" OR "PDE5" OR (CYCLIC GUANOSINE MONOPHOSPHATE (W) PHOSP
L40        6539 S (ANGIOTENSIN (L) RECEPTOR ANTAGONIST) OR (ANGIOTENSIN RECEPTO
L41          80 S L39 (L) L40
L42          17 S L41 AND HYPERTENS?
L43          16 S L42 NOT L33
L44         115 S L31 OR L41
L45          15 S L44 AND (ANGINA? OR STROKE? OR DIABET? OR CONGESTIVE HEART FA
L46          11 S L45 NOT L43
L47           6 S L46 NOT L33
L48           5 S L46 NOT L47
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      FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS' ENTERED AT 12:19:37 ON 02 MAR 2005
L49          7998 S (SILDENAFIL? OR VIAGRA? OR TADALAFIL? OR "IC-351" OR "IC 351"
L50          7998 S (SILDENAFIL? OR VIAGRA? OR TADALAFIL? OR "IC-351" OR "IC 351"
L51          7887 S (CANDESARTAN OR "CV-11974" OR "CV 11974" OR "CV11974" OR EPRO
L52         18908 S LOSARTAN? OR COZAAR? OR "DUP-753" OR "DUP 753" OR "DUP753" OR
L53         26692 S SARALASIN? OR "P-113" OR "P 113" OR "P113" OR TELMISARTAN? OR
L54         48656 S L51 OR L52 OR L53
L55           130 S L50 AND L54
L56            46 S L55 (L) (HYPERTENS? OR (HIGH BLOOD PRESSURE? OR ELEVATED BLOO
L57            45 DUP REM L56 (1 DUPLICATE REMOVED)
L58            46 S L55 AND HYPERTENS?

=> s l55 and (angina? or stroke? or diabet? or congestive heart failure?)
L59            28 L55 AND (ANGINA? OR STROKE? OR DIABET? OR CONGESTIVE HEART FAILU
                  RE?)

=> dup rem l59
PROCESSING COMPLETED FOR L59
L60            27 DUP REM L59 (1 DUPLICATE REMOVED)
                  ANSWER '1' FROM FILE MEDLINE
                  ANSWERS '2-16' FROM FILE EMBASE
                  ANSWERS '17-27' FROM FILE WPIDS

=> d l60 1-27 ti

L60  ANSWER 1 OF 27     MEDLINE on STN                    DUPLICATE 1
TI   Interactions between grapefruit juice and cardiovascular drugs.

L60  ANSWER 2 OF 27  EMBASE  COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
     on STN
TI   New drugs approved by the FDA; New dosage forms and indications; Agents
     pending FDA approval; Significant labeling changes related to safety.

L60  ANSWER 3 OF 27  EMBASE  COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
     on STN
TI   Highlights of the year in JACC 2004.

L60  ANSWER 4 OF 27  EMBASE  COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
     on STN
TI   ACC/AHA guidelines for the management of patients with ST-elevation
     myocardial infarction - Executive summary: A report of the American
     College of Cardiology/American Heart Association Task Force on Practice
     Guidelines (writing committee to revise the 1999 guidelines for the
     management of patients with acute myocardial infarction).

L60  ANSWER 5 OF 27  EMBASE  COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
     on STN
TI   Gateways to Clinical Trials: July/August 2004.

L60  ANSWER 6 OF 27  EMBASE  COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
     on STN
TI   [New advances in drug therapy in 2003-2004].
     ACTUALITES THERAPEUTIQUES 2003-2004 (1).

L60  ANSWER 7 OF 27  EMBASE  COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
     on STN
TI   Erectile dysfunction: A need for greater awareness.

L60  ANSWER 8 OF 27  EMBASE  COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
     on STN
TI   Diastolic dysfunction.

L60  ANSWER 9 OF 27  EMBASE  COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
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on STN
TI Active drug metabolites in drug development.

L60 ANSWER 10 OF 27 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
TI [Activities of the CPMP].
AKTIVITATEN DES CPMP.

L60 ANSWER 11 OF 27 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
TI [New advances in drug therapy in the year 2002].
ACTUALITES THERAPEUTIQUES 2002.

L60 ANSWER 12 OF 27 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
TI Opinion and evidence in cardiovascular therapeutics.

L60 ANSWER 13 OF 27 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
TI BMS takes Vanlev to the FDA.

L60 ANSWER 14 OF 27 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
TI Lercanidipine: A novel dihydropyridine calcium-channel blocker.

L60 ANSWER 15 OF 27 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
TI Highlights of the **Diabetes** UK Annual Professional Meeting: 4-6 April 2001, Glasgow.

L60 ANSWER 16 OF 27 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
TI **Sildenafil** (**viagra**ρ): Use and precautions in patients with cardiovascular disease.

L60 ANSWER 17 OF 27 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
TI Composition useful for the treatment of e.g. **diabetes** comprises specific glipizide particles or its salt and at least one surface stabilizer.

L60 ANSWER 18 OF 27 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
TI Combination useful for treating hypertension, **congestive heart failure** and **diabetes** comprises a cyclic guanosine monophosphate specific phosphodiesterase type 5 inhibitor and an angiotensin II receptor antagonist.

L60 ANSWER 19 OF 27 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
TI New 3-(1-(3-(1,3-benzothiazol-6-yl) propylcarbamoyl)cycloalkyl) propianic acid derivatives are neutral endopeptidase enzyme inhibitors useful for the treatment of e.g. **stroke**, glaucoma, obesity, metabolic disease and epilepsy.

L60 ANSWER 20 OF 27 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
TI Nifedipine composition used for treating **angina** pectoris and hypertension, includes particles of nifedipine or its salt, and surface stabilizer.

L60 ANSWER 21 OF 27 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
TI Treatment of vascular condition e.g. sexual dysfunction, atherosclerosis involves administrating a combination of at least two agents selected from anti-pressor agent, endothelin antagonist and sex hormone.

L60 ANSWER 22 OF 27 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
TI New polycyclic guanine derivatives useful for treating urological,

vascular and pulmonary disorders.

L60 ANSWER 23 OF 27 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
TI Production of cationic non-viral delivery vehicle useful e.g. for DNA lipofection or targeted drug delivery, by conjugating steroid or other drug with polyamine and mixing with lipid.

L60 ANSWER 24 OF 27 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
TI Bioerodible, water-soluble, carrier device for loading or delivering drug or active agent, comprises non-bioadhesive backing layer, bioadhesive layer and composition comprising active ingredient.

L60 ANSWER 25 OF 27 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
TI Propellant free buccal spray composition used for increasing rapid absorption of active compounds, comprises active compound such as antiarrhythmic, antihypertensive, heart regulator or vasodilator and polar solvent.

L60 ANSWER 26 OF 27 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
TI Solid composition for delivery of active agents e.g. glyburide comprises carrier optionally containing a substrate having an encapsulation coat containing hydrophilic surfactants e.g. polyoxyethylene alkylethers.

L60 ANSWER 27 OF 27 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
TI Treating senescence induced hypoxia of liver using vasodilating agent.

=> save
ENTER L#, L# RANGE, ALL, OR (END):all
ENTER NAME OR (END):110603369/l
L# LIST L1-L60 HAS BEEN SAVED AS 'L10603369/L'

=> d cost

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
CONNECT CHARGES	66.39	85.90
NETWORK CHARGES	2.10	5.16
SEARCH CHARGES	0.00	266.02
DISPLAY CHARGES	32.75	170.55
FULL ESTIMATED COST	101.24	527.63

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-37.96

IN FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS' AT 12:40:23 ON 02 MAR 2005

=> d his

(FILE 'HOME' ENTERED AT 11:49:08 ON 02 MAR 2005)

FILE 'CAPLUS' ENTERED AT 11:49:13 ON 02 MAR 2005
E FOX DAVID/AU
L1 69 S E2-E3, E20-E22
E HUGHES BERNADETTE/AU
L2 22 S E3-E4
E HUGHES B/AU
L3 40 S E3
E FOX D/AU
E FOX D?/AU
E FOX D/AU
L4 75 S E3

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L5          144 S L1 OR L4
L6           62 S L2 OR L3
L7          204 S L5 OR L6
L8           10 S L7 AND HYPERTENSI?
L9            0 S L7 AND (CYCLIC GUANOSINE MONOPHOSPHATE (W) (PHOSPHODIESTERASE
L10           6 S L7 AND ("CGMP" OR "PDE5" OR "ANGIOTENSIN II RECEPTOR ANTAGONI

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L14           1 S CANDESARTAN/CN
                 E CANDESARTAN/CN
L15           2 S E3-E5
                 E EPROSARTAN/CN
L16           2 S E3-E5
                 E IRBESARTAN/CN
L17           4 S E3-E6
                 E LOSARTAN/CN
L18           4 S E3-E7
                 E OLMESARTAN/CN
L19           2 S E3-E5
                 E SARALASIN/CN
L20           2 S E3-E4
                 E TELMISARTAN/CN
L21           5 S E3-E7
                 E VALSARTAN/CN
L22           2 S E3-E4
L23           6 S L11 OR L12 OR L13
L24          23 S L15 OR L16 OR L17 OR L18 OR L19 OR L20 OR L21 OR L22

     FILE 'CAPLUS' ENTERED AT 12:02:01 ON 02 MAR 2005
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                 E HYPERTENSION/BI
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                 E HYPERTENSION/CT
L28       43383 S E3
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L30       80818 S L29 OR (HIGH BLOOD PRESSURE) OR (ELEVATED BLOOD PRESSURE) OR
L31          36 S L25 AND L26
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L33           9 S L30 AND L31
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L44         115 S L31 OR L41
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L47           6 S L46 NOT L33
L48           5 S L46 NOT L47

     FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS' ENTERED AT 12:19:37 ON 02 MAR 2005
L49        7998 S (SILDENAFIL? OR VIAGRA? OR TADALAFIL? OR "IC-351" OR "IC 351"
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L50	7998	S (SILDENAFIL? OR VIAGRA? OR TADALAFIL? OR "IC-351" OR "IC 351"
L51	7887	S (CANDESARTAN OR "CV-11974" OR "CV 11974" OR "CV11974" OR EPRO
L52	18908	S LOSARTAN? OR COZAAR? OR "DUP-753" OR "DUP 753" OR "DUP753" OR
L53	26692	S SARALASIN? OR "P-113" OR "P 113" OR "P113" OR TELMISARTAN? OR
L54	48656	S L51 OR L52 OR L53
L55	130	S L50 AND L54
L56	46	S L55 (L) (HYPERTENS? OR (HIGH BLOOD PRESSURE? OR ELEVATED BLOO
L57	45	DUP REM L56 (1 DUPLICATE REMOVED)
L58	46	S L55 AND HYPERTENS?
L59	28	S L55 AND (ANGINA? OR STROKE? OR DIABET? OR CONGESTIVE HEART FA
L60	27	DUP REM L59 (1 DUPLICATE REMOVED)
		SAVE ALL L10603369/L